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THE AMERICAN
JOURNAL OF PHARMACY

OCTOBER, 1918

EDITORIAL.

PHARMACY IN THE MELTING POT.

It may be considered as axiomatic that all progress must be paid for with a price. In the present world war for the extension of human liberty and democracy, the nations of the earth are paying a stupendous price, but who is willing to say that the world's progress that will result from this war will not be commensurate with the enormous sacrifices of blood and resources that are now being made? Out of this titantic struggle there will come a chastened world, and we may well hope with improved moral and social conditions. The effect on the arts, literature, science and industry can be only partially foretold, and its influence upon the professions and commerce is likewise problematical.

The drug trade and the practice of pharmacy will have its share in this ordeal, and we must inevitably look for some changes in the practice of pharmacy. The shortage of labor has reduced the number of drug stores and the higher educational requirements will curtail the number of those taking up the professional side of the calling. We must likewise recognize that there is a growing tendency in pharmaceutical circles for higher attainments along educational and professional lines, and this eventually will have a telling effect upon the practice of pharmacy in America.

Not the least of the conditions that will affect the future of pharmacy will be the changes which will be wrought in the practice of medicine through the demands of the army and navy for physicians, and the changes which the war is going to effect in the practice of medicine and surgery.

It has been stated that the entire world with all its industries may be considered as being in a universal melting pot, and phar-

macy is likewise going through its process of refinement and change, and those who have the hope of a professional pharmacy evolving therefrom, have faith that as a result of these various internal upheavals and exterior movements, pharmacy will be more firmly established upon a scientific professional foundation.

G. M. B.

THE OPINION OF AN EMINENT FOREIGN PHARMACEUTICAL AUTHORITY OF AMERICAN PHARMACY.

Dr. J. J. Hofman, Secretary-General of the International Pharmaceutical Federation, has recently published a review of the Pharmacopœia of the United States IX.

It is interesting to note his opinion of the United States Pharmacopœia and his impression of American pharmacy, despite some of the rather derogatory remarks of certain of our presumed leaders in American pharmaceutical circles as to the status of pharmacy in the United States. This eminent foreign pharmaceutical authority, after reviewing the various titles and subjects as treated in the several parts of the Pharmacopœia and some of the important preparations of the United States Pharmacopœia IX, makes the following comment:

"Like every pharmacopœia, the U. S. P. IX contains an historical sketch which shows how pharmacy has developed in the United States. It gives a good impression of American pharmacy, and proves that, next to good salesmanship, which distinguishes the American apothecary, the striving for substantial scientific work, coupled with a practical mind, is also held in high esteem by the pharmaceutical profession there."

G. M. B.

ERRATIC ALCOHOL LEGISLATION.

The United States Congress is commonly looked upon as a body of able legislatures who give careful consideration to the various problems presented to them, and presumably they are acquainted with the past history and precedents that should influence their action. It is difficult, indeed, to conform this estimate of the American Congress with the erratic legislation on distilled spirits which

has been decreed in the various Congressional enactments since 1862.

For some unknown reason the drug trade has been singled out for an unjust burden of taxation. In the recent Congressional enactments no other class of business men have been so heavily burdened by taxation, in proportion to the business done, as have the druggists. The War Revenue Measure, approved October 3, 1917, fixed a tax on alcohol withdrawn for non-beverage purposes at $2.20 per proof gallon. The revenue bill now under consideration by Congress proposes to make this tax on distilled alcohol for non-beverage purposes $4.40 per proof gallon. This means that the tax on alcohol used in medicinal preparations will be $8.36 per gallon.

Medicines are rightly classified along with food and clothing as among the prime necessities of life, and it is difficult to understand that any underlying principle or war necessity would dictate a policy of excessive taxation on any of these.

Drugs are collected from all over the world, and the increased war demands for many of these and the existing difficulties of transportation, shortage of labor, and the high cost of the ingredients, including the solvents necessary, have all tended toward making the cost of all medicines abnormally high, and some of those most needed are beyond the means of many of our people.

Alcohol is indispensable in the production of most medicines, and the proposition for still further increasing the cost of medicines by doubling the excise tax on the alcohol used is indefensible as an economic principle. This question is one that must finally be brought home to every consumer, and those afflicted by disease or injury must in the final analysis bear the burden of this tax.

It is doubtful whether any other nation would place such a burden of taxation upon those who must necessarily consume medicines.

A pertinent question to be considered by each member of Congress is whether he is prepared to defend before his constituents such an excessive tax on materials essential to the preservation of life and health—a tax that is contrary to all humanitarian ideas and consideration for the urgent needs of the sick and indigent. Is any one ready to declare that the exigencies of this nation demands such callous and inhuman treatment of our invalids? We are passing through one of the worst epidemics of sickness that has ever afflicted any nation, and many of the common remedies, such as sweet spirit of nitre used in the treatment of this fever in enor-

mous quantities, by reason of the alcohol tax can be supplied only at prices three or four times the normal cost. To now propose to double the tax on alcohol means practically the doubling of the already excessive prices on many of the remedies used in professional medical practice as well as in domestic treatment.

A short review of the various excise taxes upon proof spirits may not be amiss. By the Act of July 1, 1862, the excise tax on proof spirits was fixed at 20 cents per wine gallon. Under the stress of the War of the Rebellion, this was successively increased by the Acts of March 7, 1864, and June 30, 1864, to 60 cents and $1.50 per proof gallon, respectively, and by the Act of December 22, 1864, it was increased to $2.00 per proof gallon. After the war was over, it was recognized that this excessive war tax was no longer necessary and by the Act of July 20, 1868, the tax on proof spirits was fixed at 50 cents per gallon. The Act of March 3, 1875, increased this tax to 90 cents, and early in the 90's it was advanced to $1.10 per proof gallon, and the latter figure was retained until 1917, when, under the necessity for war revenue, it was doubled.

Congress, nevertheless, by various enactments, has demonstrated in the past its appreciation of the fact that the industries of the country that must necessarily use alcohol as a raw material, should not be burdened with a heavy tax on this material, and likewise that for humanitarian reasons the price of medicines should not be unnecessarily increased. In 1893, the Hoar Bill was passed, making provision for tax free alcohol for use in the arts and for medicinal preparations. This measure provided that the tax collected by the Internal Revenue Department was to be rebated to the manufacturers after regulations prescribed by the Secretary of the Treasury had been satisfactorily complied with. The Secretary of the Treasury failed to formulate regulations for making this act effective, and in 1896 it was repealed.

Congress has since reaffirmed this principle and further demonstrated its interest in certain manufacturers using alcohol as a raw material by passing the Denatured Alcohol Act of June 7, 1906, and the several later amendments thereto, by which many industries which can use the various formulas for denatured alcohol, are permitted to use alcohol in this form free of excise tax. The stumbling block in the Hoar Bill, namely, the regulations for the rebate of the tax collected was eliminated in these laws, as provision

is made therein for the withdrawal of alcohol denatured under the regulations without any payment of the excise tax on distilled spirits. There are some other manufacturers, however, such as those who manufacture pharmaceuticals, flavoring extracts, perfumery and toilet articles, who, from the very nature of their products, must have pure alcohol as a solvent because of the very necessity to preserve the standard and purity of their products. These equally important industries have been discriminated against and denied by Congressional enactments and the Treasury Department regulations the privilege of using tax free alcohol that has been extended to the other favored industries.

It is fair to assert that no other industry has such a strong appeal for freedom from taxation as the industry that supplies medicines to the needy and sick of the nation; yet, because this industry must necessarily have pure alcohol as a solvent, it is burdened with an excessive tax, which must ultimately be borne by the consumers of the medicines produced. To the pharmacists and chemical manufacturers, who produce the necessary medicines, alcohol as a solvent has no further consideration than has water or glycerin as a solvent where such is essential to the production of their products.

It will be recognized that the tax on distilled spirits has always been viewed by Congress rather as a question of revenue than as a means of producing prohibition. The moral or prohibition argument does not enter at all into the question now under consideration. A manufacturer who prepares a lacquer to preserve our ornaments or the varnish or paint to adorn and preserve our homes can have tax-free alcohol, but the pharmaceutical manufacturer who prepares medicines to preserve the human body as a suitable habitation for the soul, is denied this same privilege. A tax on the water used as a solvent would be quite as justifiable as a tax on the alcohol used for the same purpose.

G. M. B.

THE VALUE OF THE MICROSCOPE IN THE DRUG STORE.[1]

By Heber W. Youngken, Ph.G., Ph.D.

The object of this paper is to point out the advantages of the microscope as applied to the needs of the average retail pharmacist.

The writer in his frequent visits to various drug stores, has been astonished at the comparatively small number possessing microscopes, especially in view of the fact that the pharmacognostic standards for many U. S. P. and N. F. drugs are very exacting. This condition is not without a reason. He has therefore inquired of students and pharmacists why the microscope is not made use of in determining the purity of the various crude, granulated and powdered drugs and spices handled. Several have essayed it to be something non-essential because they deal with reputable houses. Others have admitted it to be of value but claim the time required to examine drugs microscopically would be out of proportion to the profits accrued.

I am well aware that all thinking business men measure their time in terms of dollars and cents and so, if they can be shown a way to make the dollars, they will surely grasp it.

Two of the telling points in business are confidence and service. There must be confidence on the part of the purchaser that the article for sale is worth what is asked for it and, moreover, that it is exactly what is asked for. A dissatisfied customer will seldom return. To secure the confidence of one's customers is more essential in the pursuit of pharmacy than practically any other line of business enterprise. The very fact that the public is aware of the poisonous nature of a number of drugs makes it alert to view any mistake made by the pharmacist as an act of gross incompetence. Quite frequently, minor errors on the part of pharmacists have been seized upon and magnified to others with a resultant dimunition of their confidence and a consequent loss of considerable trade.

Just recently I was shown a sample of sweet marjoram purchased in a one-ounce carton from a local druggist by one of my neighbors. The neighbor contended that it was "rubbish." When

[1] Read at the annual meeting of the Pennsylvania Pharmaceutical Association, Wilkesbarre, Pa., June, 1918.

I examined it, I found that the drug was not only ancient but admixed with hair, dirt, foreign stems and a foreign leaf. Subsequent microscopical examination showed the foreign leaf to be that of *Coriaria myrtifolia,* a poisonous species, which no doubt was collected with the marjoram. Had this particular druggist purchased his stock of sweet marjoram in bulk and examined it microscopically, he would have saved this customer, for despite all the excuses I could manufacture to protect the druggist, the party vowed he would never go back to that store for anything.

This is but one example of a crude drug adulterated. Numerous others have, and still are being adulterated. Some of the most common might be cited as poke in belladonna, wafer ash bark in euonymus, ruellia in spigelia, fagot cinnamon in saigon cinnamon, European rhubarb in Chinese rhubarb, safflower in saffron, etc., etc.

Many instances can be given showing the value of the microscope in the examination of powdered drugs and spices and the detection of adulteration. For instance, the presence of saw-dust in white pine bark, powdered mullein and elecampane leaves in powdered digitalis, wheat middlings in ground ginger, powdered bombay mace in mace, the endocarp of the olive in ground black pepper, etc.

Not long ago one of my students took occasion to examine some five-grain acetyl-salicylic acid tablets microscopically, which had been purchased by his preceptor at a figure slightly below that of market quotation. He was surprised to find in these considerable corn starch. A quantitative analysis later made by his preceptor showed that the five-grain tablets were composed of three grains of acid acetyl-salicylic and two grains of corn starch. This is but one of the numerous cases that might be cited to show the value of the microscope in determining the purity of chemicals.

Much of what I have thus far shown bears upon the value of the microscope in determining the authenticity of the article. Let us now turn to the money side of the question. This naturally has a strong bearing upon the quality of drugs sold.

Some of our more scrupulous brethren in pharmacy are modestly and quietly examining samples of the drugs they handle and no doubt reaping their reward by the reputation they have gained for handling and dispensing effective medicaments. But how much greater might be the returns, if they were to *advertise the fact* alike to the laity, and to the medical profession.

This could be accomplished through the medium of the press, by

having cards posted in conspicuous places about the store, announcing the fact that all drugs entering the store were examined carefully before being dispensed and by placing the microscope in the show window when not in use, accompanied by a neatly printed card explaining the use made of the instrument in passing upon the drugs handled. This form of advertising would soon attract considerable attention and aid in giving the drug store that professional appearance which I regret to state many of the so-called modern drug stores sadly lack.

When the care exercised in selecting and handling drugs and spices becomes generally known to the public, I venture to say that the pharmacist's trade would be greatly augmented. He would further be able to charge and obtain more for his medicines on the basis of professional services rendered.

Finally, the microscope is a valuable asset because its use protects the druggist from incrimination. The Pure Food and Drug Acts of the National and State Governments make it incumbent upon all dealers in drugs and chemicals to sell and dispense only such U. S. P. and N. F. drugs which conform to the standards of the U. S. P. IX and N. F. IV. The Federal and State inspectors may drop in at any time and generally the least expected one.

The mere labelling of a package of ground, powdered or crude drug by the wholesaler, as conforming to the Drug Act does not save the pharmacist from prosecution in case of adulteration, once the package or carton has been opened by him. For an unscrupulous wholesaler could claim that the contents were tampered with by the retailer.

Many will doubtless say, "We can protect ourselves by only handling drugs in cartons sealed and labelled by the wholesaler." Unfortunately for such, that cannot be done in every case of a drug called for, as verified by practical experience.

The druggist not examining his drugs, therefore, makes himself subject to prosecution at any time he sells or dispenses a misbranded article.

It can readily be conjectured through the sad experience of others what effect such prosecution would have upon the reputation of the store and confidence of its customers. Once these have been lost the druggist might as well prepare to move.

I know of no other start to bring pharmacy back to its own than to practice it as it should be practised. Anything worth doing is

worth doing well, and he who does it well is duly rewarded, not only in dollars, but in that state of mind which one of our philosophers states to be the main purpose of life, namely, happiness.

THE DETERMINATION OF MORPHINE IN COMPLEX PRODUCTS.[1]

PART I. A REVISION OF THE ANALYTICAL REACTIONS EMPLOYED.

BY ALFRED TINGLE, PH.D.

CHEMICAL LABORATORY, DEPARTMENT OF CUSTOMS, OTTAWA, CANADA.

INTRODUCTION.

Laws aiming at the restraint of the morphine habit in its various forms have been enacted in every civilized country. Consequently, official chemists may be called upon at any time to decide whether morphine is contained in some pseudo-medicinal preparation and to determine its amount. The question arises most frequently in Asiatic countries or in those which receive Asiatic immigrants. In such cases the chemist's task is made more difficult by the fact that the material to be examined is likely to be of Asiatic manufacture and mysterious composition. The problem has been a recurring one to the writer for nearly nine years, commencing with the time when he was attached to a Bureau for the Suppression of Opium Smoking under the Chinese Government. No method to be followed in such cases seems to have been published, but experience has shown the practical need of one.

In the course of his endeavors to supply this want the writer has found so many of the statements made in the literature about morphine to be mutually contradictory, or based on imperfect evidence, that it became necessary to take for granted as little as possible. Some reactions which might have a bearing on the analytical behavior of this base have been studied hitherto only as they throw light on its constitution and not on the quantitative side. All the data pertinent to the present investigation have therefore been carefully revised, and the results are here briefly set forth. A method has been devised, founded on these data, by which morphine in

[1] Read by title at the meeting of the Royal Society of Canada.

medicinal preparations may be accurately determined. This method, or obvious modifications of it, has a very wide range of applicability —the more so, since it calls for no arbitrary "corrections," but rests on strictly stoichiometrical relations. It cannot be used, however, when the morphine is present in the form of opium. To meet such cases a modification has been devised. This latter can also be used for the examination of opium itself, and is more accurate than the methods at present in use. As a matter of convenience these will be presented in separate communications.

Discussion of the Analytical Data Obtained.

Acidimetric Titration of Morphine.—When morphine is dissolved in standard sulphuric acid and the excess of acid is determined by titration with a caustic alkali solution, the amount of morphine may be calculated directly from its molecular weight. Contrary to some statements, and to the writer's own previous belief, it is not necessary to standardize the acid on the alkaloid itself. Some of the writer's earlier experiments did not bear out this view, but it was later found that the acid used had been standardized by a faulty method. By Experiment 1 (see subsequent pages) it is shown that 1 Cc. $\frac{N}{10}$ H_2SO_4 = 0.0304 Gm. $C_{17}H_{19}NO_3 \cdot H_2O$ and while theory calls for less by 0.0001 Gm., the difference is within the limit of observational error, so that the theoretical figure 0.0303 should be used. That methyl orange gives the same end point as other suitable indicators in this reaction is shown by Experiment 2, but the correct end point for methyl orange is not the one usually used and is difficult to find with the unaided eye. It is best found by using the spectroscopic method. (*Jour. Amer. Chem. Soc.*, XL, 1918. 873.)

Iodometric Titration of Morphine.—This consists in adding a known volume of decinormal iodine solution to an acid solution of the alkaloid. The resulting per-iodide is filtered out and the excess of iodine determined in an aliquot portion of the filtrate (Prescott and Gordin, *Jour. Amer. Chem. Soc.*, XX, 727). The great value of this method lies in the fact that by it morphine may be determined without being first separated as a free base. So many substances interfere with its applicability, however, as to greatly decrease its value. Its reliability has fallen under suspicion through attempts to apply it to other alkaloids which do not react with iodine in the same

way. Experiment 3 shows that the reaction is strictly quantitative, and that the iodine solution need not be standardized directly on morphine.

Iodo-Acidimetric Titration of Morphine.—This method, proposed by Gordin (*Pharm. Archives,* 1899, 2, 313–318) appears so plausible that it finds a place in works on alkaloidal assays, despite Kippenberger's destructive criticism (*Zeit. Anal Chem.* 42, 101–108). Experiment 4 leads to the belief that the sodium tetrathionate formed in the course of the reaction is partly responsible for its entire unreliability.

Extraction of Morphine by Solvents Immiscible with Water-Chloroform-Alcohol Mixtures.—Many solvents have been proposed for the extraction of morphine. Most offer great practical disadvantages. Some are extremely apt to form emulsions with alkaline liquids. others are specifically lighter than water, so that their use entails greater manipulative losses. Those of high boiling-point are very objectionable, as the morphine can only be quantitatively separated from them by re-solution in acid. None of these disadvantages adhere to chloroform-alcoholic mixtures. The writer prefers to use 2 volumes of chloroform to 1 volume of alcohol, as advocated by J. B. Williams (*Amer. Jour. Pharm.,* 1914, 86, 308–312). That four extractions, made under the conditions there defined, will completely separate morphine, is shown by Experiments 5 and 6. The very slight deficiency of morphine at the end of these experiments is within the limit of error due to manipulation, etc., and direct tests establish that no alkaloid was left in the aqueous solution. W. A. Puckner (*Jour. Amer. Chem. Soc.,* 1901, XXIII, 470–473) deprecates the use of ammonium hydroxide for the liberation of morphine, but it should be remarked that his gravimetric determinations were admittedly of no value, while the errors attributed to the use of ammonium hydroxide rather than sodium bicarbonate are less than the smallest error that his volumetric method could detect. He worked with chloroform-alcohol mixtures in which the proportion was 4:1. Kippenberger has published some observations on this subject (*Zeit. Anal. Chem.,* XXXIX, 290), but his paper is not accessible to the present writer. Chloroform-alcohol mixtures extract small quantities of morphine from solution even in the presence of alkaline hydroxides or free mineral acid. In the latter case the morphine is extracted in the form of a salt, as proved by Experiment 7.

Precipitation of Morphine by Ammonium Hydroxide under Various Conditions. Sources and Extent of Loss.—Most standard methods for the determination of morphine depend on its precipitation from acid solution by addition of an excess of ammonium hydroxide or, what amounts to the same thing, from alkaline solution by ammonium chloride. In the majority of such cases alcohol is also added. It is difficult or impossible to precipitate morphine in reasonably pure condition from any solution containing resinous matter without the use of an organic solvent to retain the latter. This precipitation of morphine is never quantitative, and some experiments have been made to exhibit clearly the extent of the errors involved, and their source.

The conditions of Experiment 8 were arranged to conform as nearly as possible to those under which morphine is thrown down in Stevens's assay of opium (*Pharm. Arch.*, V, 41–45). The result closely confirms Stevens's estimate of the losses involved. A mixture of 30 Cc. of water with 8 Cc. of alcohol dissolves 0.05 Gm. of the alkaloid. From Experiments 9 and 10 taken together it may be deduced that variations in the amount of free ammonium hydroxide or of ammonium salts have little effect on the solubility of morphine. The volume of dilute alcohol is the same in both cases, as is (within limit of error) the loss of alkaloid. But while the volume of liquid is only one third of that used in Experiment 8, the morphine held in solution is proportionately more. This is to be accounted for in part by the fact that the precipitates were washed with water instead of a saturated aqueous solution of morphine.

That water has an appreciable solvent action in the morphine is clearly shown in Experiments 12 and 13, though the action is very slight in comparison with that of alcohol. The results of these experiments are in fair agreement with those calculated from the more recent of the very conflicting data on the solubilities of this alkaloid.

Experiment 11 shows that morphine can be precipitated from an aqueous liquid with little more loss in the presence than in the absence of chloroform, and that the precipitation can be effected in a reasonably short time.

Taken all together the writer claims to have shown (1) That the principal loss of morphine in this precipitation is due to alcohol (2) That ammonium salts and ammonia play only a very secondary part. (3) That a long precipitation period is not necessary. (4) That a fairly complete precipitation can be effected in the presence

of chloroform and water in a short time. (5) That washing with "morphinated" water only becomes necessary when large volumes are employed.

It is therefore logical to avoid, when possible, the precipitation of morphine in the presence of alcohol. If the latter solvent is used, even approximately quantitative results cannot be obtained.

The Actoin of Barium Hydroxide on Solutions which contain Salts of Morphine.—Many secondary authorities state that morphine is soluble in barium hydroxide solution, but they give no references. While the statement was inherently probable, the point became one of such great importance that it was necessary to verify it. Experiments 14 and 15 show that barium hydroxide dissolves morphine and that the latter is not thus precipiated to any important extent by an excess of sulphuric acid or by starch. Even a large excess of barium hydroxide, however, will not bring morphine completely into solution in the presence of lead, as is shown by Experiment 16. This point is one of practical importance.

Action of Ammonium Salts on Morphine.—It is no new observation that morphine liberates ammonia when evaporated with solutions of ammonium salts, but Experiment 17 was made to show the extent to which this action might produce an analytical error. That the same action is appreciable even at the ordinary temperature is shown by Puckner's results (*loc. cit.*) on the extraction of morphine from its solutions in the presence of a large excess of ammonium chloride.

The Action of Acids on Morphine.—It is well known that several of the stronger acids act on morphine under certain conditions, forming apo-morphine and other derivatives, but the limits of these reactions have not been studied. It is therefore important to know whether morphine is acted upon by these acids under analytical conditions; whether, for instance, appreciable loss of alkaloid will result from evaporation with a certain acid on the water bath. Experiments 18, 19, 20 and 21 indicate that some change occurs when morphine is heated on the water bath, under such conditions as might occur in the course of an analysis, with dilute sulphuric and acetic acids, but that no such change is produced by hydrochloric or salicylic acids. All analytical procedure must be regulated accordingly.

The Reactions of Morphine Tartrate.—A. W. and M. W. Blyth (Poisons: Their Effects and Detections, 4th edition, p. 297) state

that morphine tartrate might escape detection "if the expert trusted alone to the usual test of an alkaloidal salt giving a precipitate when the solution is alkalized by the fixed or volatile alkalies; for the tartrates of morphine do not give this reaction, nor do they give any precipitate with calcic chloride." A somewhat similar statement is made in Allen's "Commercial Organic Analysis," 4th (American) edition, Vol. VI, p. 378. No original authority is quoted on the point in either of these works. On the other hand, the British Pharmacopœia states that normal morphine tartrate (Morphinæ Tartras B. P.) gives the usual reactions of morphine salts and of tartrates. The discrepancy between such standard works of reference is a serious one, and under certain circumstances might have unfortunate results. The point raised has, besides, considerable theoretical interest, if the statements of Messrs. Blyth are correct. It is shown by Experiment 22 that the British Pharmacopœia is substantially to be relied on in this matter, and that the assertions in the other two works quoted are not well founded. It would be interesting, if possible, to follows these errors to their source.

The facts above-mentioned as re-established are the basis of the analytical methods to be described in Parts II and III of this communication.

Experimental Data on the Analytical Behavior of Morphine.

Strength of $\frac{N}{10}$ H_2SO_4 in Terms of Crystallized Morphine, $C_{17}H_{19}NO_3 \cdot H_2O$. Experiment 1.—The acid used was standardized against tartaric acid (Babington and Tingle, *Jour. Soc. Chem. Ind.*, XXXVI, 203–204) and was found to be $\frac{N}{10} \times 1.0032$. The crystallized morphine was purified with unusual care. After weighing it was dissolved in a measured volume of acid, and the solution was titrated against standard sodium hydroxide, lacmoid being the indicator.

Total acid used	= 25.00	Cc.
Acid equivalent to the alkali	= 5.38	Cc.
Acid equivalent to the morphine	= 19.62	Cc.
Weight of morphine used	= 0.6000	Gm.

Consequently 1 Cc. of above acid = 0.03058 Gm. of morphine or 1 Cc. $\frac{N}{10}$ acid = 0.0304 Gm. of morphine, while theory requires

0.0303 Gm., the difference being within the limits of measurement error.

The Effect of Different Indicators on Titrations of Morphine with Sulphuric Acid. Experiment 2.—Two portions of crystallized morphine (0.3000 Gm. each) were dissolved separately in measured volumes of sulphuric acid, the excess of which was titrated with standard sodium hydroxide.

	Lacmoid Indicator.	Methyl Orange Indicator.
Total acid used	= 25.00 Cc.	25.00 Cc.
Acid equivalent to the alkali	= 15.13 Cc.	15.16 Cc.
Acid equivalent to the morphine	= 9.87 Cc.	9.84 Cc.

The discrepancy between the results obtained with these two indicators was therefore 0.03 Cc. of $\frac{N}{10}$ acid, a quantity within the limit of the errors of measurement. In the titration in which methyl orange was used, the end point was observed spectroscopically according to the method described by the writer (*Jour. Amer. Chem. Soc.*, XL, 1918. 873).

Strength of $\frac{N}{10}$ Iodine Solution in Terms of Anhydrous Morphine $C_{17}H_{19}NO_3$. Experiment 3.—The solutions of iodine and sodium thiosulphate were compared with one another. The latter was standardized against potassium bichromate and acidified potassium iodide.

The iodine solution was thus found to be $\frac{N}{10} \times 0.9692$. Purified anhydrous morphine was weighed, dissolved in acid and diluted to such volume that 100 Cc. of the solution contained 0.5336 Gm. of base.

To 25 Cc. of this solution 25 Cc. of standard iodine solution was added. The mixture underwent no change of volume. It was shaken and filtered through glass wool. In 25 Cc. of the filtrate the excess of iodine was determined by titration with sodium thiosulphate.

$Na_2S_2O_3$ used = 5.28 Cc. standard iodine.. Therefore morphine in 12.5 Cc. of morphine solution = 7.22 Cc. standard iodine. Therefore 1 Cc. of $\frac{N}{10} \times 0.9692$ iodine solution = 0.00923 Gm. of anhydrous morphine.

Theory requires 1 Cc. = 0.00920 Gm.

Alkalimetric Measurement in Presence of Sodium Tetrathionate. Experiment 4.—A. A slight excess of sodium thiosulphate was added to 50 Cc. of $\frac{N}{10}$ iodine solution. A measured volume of standard

sodium hydroxide solution was added to the tetrathionate thus formed. This was then titrated with $\frac{N}{10}$ sulphuric acid, the indicator being phenolphthalein.

B. A titration was made as in the previous case, but the tetrathionate present was that yielded by 100 Cc. of $\frac{N}{10}$ iodine solution.

C. A measured volume of the standard alkali was added to 50 Cc. of the sodium thiosulphate solution used above. It was then titrated as in A and B.

D. A blank experiment was made in which the standard alkali was titrated against $\frac{N}{10}$ acid without any previous admixture. Titration results:

	A.	B.	C.	D.
NaOH solution used	25.00 Cc.	25.00 Cc.	25.00 Cc.	25.00 Cc.
$\frac{N}{10}$ H_2SO_4 required to neutralize ..	10.65 Cc.	9.90 Cc.	12.00 Cc.	12.00 Cc.

The neutrality of the iodine solution used in the above experiments was shown by taking 50 Cc., adding just enough sodium thiosulphate to decolorize it, and testing the resulting solution with lacmoid, methyl orange and cochineal. With all these it gave a neutral reaction.

The Extraction of Morphine by a Mixture of Chloroform and Alcohol (2 : 1). *Experiment* 5.—Crystallized morphine (0.3000 Gm.) was dissolved in dilute sulphuric acid. The solution was transferred to a separating funnel, and enough ammonium hydroxide was added to make it strongly alkaline, care being taken that the total volume did not exceed 25 Cc.

The solution was well shaken for 3 minutes with 25 Cc. of a mixture of chloroform and alcohol (2 volumes of the former to 1 volume of the latter). The lower layer was separated and the extraction repeated in exactly the same way. In all, four extractions were thus made.

The united extracts were distilled on a water bath, the residue being then dissolved in standard sulphuric acid, the excess of which was later titrated with standard sodium hydroxide solution and lacmoid indicator.

[The standard acid used in this and most succeeding experiments was slightly less than $\frac{N}{10}$, being so adjusted that 1 Cc. = 0.0300 Gm. crystallized morphine.]

Total acid used	= 17.00	Cc.
Acid equivalent to the alkali	= 7.10	Cc.
Acid equivalent to the morphine	= 9.90	Cc.
Weight of morphine extracted	= 0.2970	Gm.

Loss of morphine = 0.0030 Gm, equivalent to 0.1 Cc. of standard acid.

After being extracted as above described, the aqueous layer was slightly acidified and evaporated to small volume. Tested for the presence of morphine by iodic acid, by bismuth potassium iodide and by iodine solution, this concentrate gave in each case a negative result.

Experiment 6.—Pure morphine was dissolved in standard acid. The solution was then titrated with standard sodium hydroxide solution.

Total acid used	= 25.00	Cc.
Acid equivalent to the alkali	= 15.00	Cc.
Acid equivalent to the morphine	= 10.00	Cc.

The titrated solution was faintly acidified with hydrochloric acid, evaporated almost to dryness on the water bath and transferred to a separating funnel, washing in with 10 Cc. of water and 3 Cc. of alcohol. Enough sodium hydrogen carbonate (a saturated aqueous solution) was added to make the whole distinctly but slightly alkaline. The morphine was then extracted exactly as in Experiment 5.

Titration of the residue produced the result which follows.

Total acid used	= 25.00	Cc.
Acid equivalent to the alkali	= 15.05	Cc.
Acid equivalent to the morphine	= 9.95	Cc.

Morphine apparently lost in the extraction was therefore 0.0015 Gm. (= 0.05 Cc. acid) which is within the limit of observational error.

For complete extraction of morphine by this method the initial volume of the aqueous layer should not exceed the volume of chloroform-alcohol taken for each extraction. When the former was 40 Cc. and the latter 25 Cc., it was found that four extractions left 0.018 Gm. (6 per cent.) of the base in the aqueous layer.

When 0.2727 Gm. of morphine was in 50 Cc. of solution it was completely extracted by shaking four times with 50 Cc. of chloroform-alcohol mixture.

Extraction of Morphine Salts by a Mixture of Chloroform and Alcohol. Experiment 7.—Crystallized morphine (0.3000 Gm.) was dissolved in dilute sulphuric acid. The solution was made alkaline by sodium hydroxide, then faintly acid with hydrochloric acid. This acid mixture was then extracted four times with chloroform-alcohol exactly as were the alkaline solutions in Experiments 5 and 6. The extracts were combined, the chloroform and alcohol distilled on a water bath and the residue set aside for further examination.

The acid aqueous layer was made slightly alkaline with sodium hydrogen carbonate and again extracted four times with the same solvent as before. The residue from these extractions was set aside for further examination.

Acid Extract.—This dissolved almost completely in water, leaving only a slight oily cloud of insoluble matter (chloroform?). The solution was acidified with standard acid and titrated with sodium hydroxide.

Total acid added	= 5.00 Cc.
Acid equivalent to the alkali used	= 5.15 Cc.

A trace of free acid (= 0.15 Cc. $\frac{N}{10}$) was therefore contained in the extract.

After titration, the lacmoid was precipitated by adding a little slaked lime. The solution was filtered, acidified, and tested with decinormal iodine solution. The formation of a characteristic precipitate demonstrated the presence of morphine.

Alkaline Extract.—This was dissolved in a known amount of standard sulphuric acid. The solution was titrated with standard sodium hydroxide.

Total acid used	= 15.3 Cc.
Acid equivalent to the alkali	= 6.4 Cc.
Acid equivalent to the morphine	= 8.9 Cc.

The morphine extracted from the alkaline solution was therefore 0.2670 Gm., so that 0.0330 Gm. must have been extracted from the acid solution in the form of a salt by the chloroform-alcohol mixture.

Precipitation of Morphine by Ammonium Hydroxide under Various Conditions. Experiment 8.—Crystallized morphine was weighed into a stoppered flask and dissolved in 25 Cc. of $\frac{N}{10}$ sulphuric acid. To this was added 8 Cc. of alcohol, 20 Cc. of ether

and 5 Cc. of dilute ammonium hydroxide. The now alkaline mixture was well shaken, then allowed to stand over night. It was filtered through a cotton plug and washed with 20 Cc. of ether and a sufficient quantity of morphinated water, in the manner laid down by Stevens for the assay of opium (*Pharm. Arch.*, 1903, V, 41–45). The cotton plug was transferred back to the precipitation flask, into which all morphine in the funnel was washed by a stream of $\frac{N}{10}$ sulphuric acid. When all the morphine had dissolved in this measured quantity of acid, the solution was titrated with standard sodium hydroxide, lacmoid being the indicator.

Total acid used in titration	= 25.00 Cc.
Acid equivalent to the alkali	= 12.88 Cc.
Acid equivalent to the morphine	= 12.12 Cc.

This corresponds to 0.3672 Gm. morphine found.

Weight of morphine originally taken	= 0.4172 Gm.
Loss in precipitation	= 0.0500 Gm.

Experiment 9.—In this case also precipitation was effected in the presence of alcohol and ether, but the total volume of solution was smaller, and the amount of ammonium hydroxide in excess was observed. Crystallized morphine was weighed into a stoppered flask and dissolved in 2.5 Cc. *N* sulphuric acid. To this 2.5 Cc. of alcohol, 10 Cc. of ether and 7.5 Cc. of 0.36 *N* ammonium hydroxide were added successively. The manipulation which followed was the same as in Experiment 8, except that the washing was conducted with distilled water (10 Cc.) instead of water saturated with morphine.

Since 1 Cc. of this standard acid = 0.0300 Gm.

Titration results:

Total acid used	= 15.00	Cc.
Acid equivalent to the alkali	= 5.80	Cc.
Acid equivalent to the morphine	= 9.20	Cc.
Since 1 Cc. of this standard acid	= 0.0300	Gm. morphine
Weight of morphine found	= 0.2760	Gm.
Weight of morphine originally taken	= 0.3000	Gm.
Loss in precipitation	= 0.0240	Gm.

Experiment 10.—The excess of ammonium hydroxide used in precipitation was larger, but the total amount of ammonium salt

present was smaller, in this than in the preceding experiment. Morphine was dissolved in 2.0 Cc. *N* sulphuric acid and precipitated by 8.0 Cc. of $\frac{55}{100}$ *N* ammonium hydroxide in the presence of 2.5 Cc. of alcohol and 5.0 Cc. of ether. The remainder of the manipulation resembled that of Experiment 9.

Titration results:

Total acid used	= 15.00	Cc.
Acid equivalent to the alkali	= 5.75	Cc.
Acid equivalent to the morphine	= 9.25	Cc.
Since 1 Cc. of this standard acid	= 0.0300	Gm. morphine
Weight of morphine found	= 0.2775	Gm.
Weight of morphine originally taken	= 0.3000	Gm.
Loss in precipitation	= 0.0225	Gm.

Experiment 11.—In this case neither alcohol nor ether were present during the precipitation, their place being taken by chloroform. The time allowed for precipitation was greatly reduced.

Crystallized morphine (0.3000 Gm.) was dissolved in $\frac{N}{10}$ sulphuric acid and the solution was titrated with standard sodium hyroxide.

Total acid used	= 25.00	Cc.
Acid equivalent to the alkali	= 15.13	Cc.
Acid equivalent to the morphine	= 9.87	Cc.

A drop of hydrochloric acid was added to the titrated solution, which was then evaporated to dryness. The residue was dissolved in 5.0 Cc. of water, to which was then added 5.0 Cc. of chloroform and enough strong ammonium hydroxide solution to make the mixture alkaline. Crystallization of morphine was promoted by stirring the liquid and scratching the sides of the containing vessel with a rod. It was allowed to stand 3½ hours from the first appearance of a precipitate. It was then filtered through a cotton plug and the morphine washed with 10–15 Cc. of water. The morphine was dissolved in dilute acid. The acid solution, with the cotton plug, was transferred to a separating funnel, made alkaline, and extracted as in Experiment 5. The morphine thus separated was titrated with $\frac{N}{10}$ sulphuric acid and sodium hydroxide.

Total acid used	= 26.50	Cc.
Acid equivalent to the alkali	= 16.89	Cc.
Acid equivalent to the morphine	= 9.61	Cc.

Comparing this with the titration made at the outset of the experiment, the loss of morphine is equivalent to 0,26 Cc. of standard acid or 0.0078 Gm. of base. Since the extraction by chloroform-alcohol is quantitative, this is loss by precipitation from solution in 5 Cc. of water in presence of 5 Cc. of chloroform.

Experiment 12.—Precipitation was effected in the presence of water only, no organic solvent being employed. Crystallized morphine was dissolved in 2.0 Cc. *N* sulphuric acid. To this was added 8 Cc of $\frac{55}{100}$ *N* ammonium hydroxide. The precipitate was allowed to form while standing over night. The remainder of the manipulation resembled that in Experiment 8, but distilled water was used to wash the precipitate.

Titration results:

Total acid used	= 15.00 Cc.
Acid equivalent to the alkali	= 8.55 Cc.
Acid equivalent to the morphine	= 6.45 Cc.
Weight of morphine found	= 0.1935 Gm.
Weight of morphine originally taken	= 0.2000 Gm.
Loss in precipitation	= 0.0065 Gm.

Experiment 13.—A weighed quantity of pure crystallized morphine was shaken and allowed to stand over night with 5 Cc. of water and 10 Cc. of well-washed ether. It was then filtered, without washing, through a cotton plug.

The undissolved residue was titrated.

Total acid used	= 21.1 Cc.
Acid equivalent to the alkali	= 11.3 Cc.
Acid equivalent to the morphine	= 9.8 Cc.

The filtrate was also titrated.

Total acid used	= 2.5 Cc.
Acid equivalent to the alkali	= 2.3 Cc.
Acid equivalent to the morphine	= 0.2 Cc.

From the above we find

Weight of morphine undissolved	= 0.2940 Gm.
Weight of morphine dissolved	= 0.0060 Gm.

Since the weight of morphine originally taken was 0.3000 Gm., a perfect balance is thus established.

The Action of Barium Hydroxide on Solutions Which Contain Salts of Morphine. Experiment 14.—A preliminary qualitative observation showed that pure crystallized morphine dissolved quickly and completely when added to a clear cold solution of barium hydroxide. The following observations show (i) that this action is quantitative and that barium hydroxide does not precipitate morphine from its solution, and (ii) that when barium sulphate is precipitated from an acid solution it carries down no morphine salt with it.

(i) From a stock solution of morphine hydrochloride 50 Cc. was taken and diluted to 100 Cc. by adding a clear cold saturated solution of barium hydroxide. The mixture was allowed to stand, protected from the air, for three hours, then filtered through a dry paper. From the filtrate 50 Cc. was taken. To it was added in succession 50 Cc. of dilute sulphuric acid, 50 Cc. of standard iodine solution and enough water to make the total volume 200 Cc. When the periodide had become crystalline it was filtered through glass wool and 50 Cc. of the filtrate was titrated with standard sodium thiosulphate solution.

(ii) To the same quantity of the same stock solution of morphine hydrochloride 5 Gm. of crystallized barium hydroxide was added. The mixture was allowed to stand over-night, then acidified with sulphuric acid, diluted to 100 Cc. and filtered through a dry paper. To 50 Cc. of this filtrate, 50 Cc. of standard iodine solution was added. The mixture was later filtered through glass wool and 25 Cc. of the filtrate was titrated with standard sodium thiosulphate solution.

(iii) A blank experiment was made using the same quantities as in (i) but substituting distilled water for the barium hydroxide solution.

In all three cases the volume of filtrate titrated corresponded to the same volume of morphine hydrochloride solution.

Titration results:

Volume of sodium thiosulphate solution required to decolorize:
(i) = 9.45 Cc. (ii) = 9.50 Cc. (iii) = 9.40 Cc.

The agreement of the results may be considered very satisfactory when the error introduced by the large amount of barium sulphate precipitate is taken into consideration.

Experiment 15.—The question was raised as to whether, when starch is precipitated by barium hydroxide in the presence of morphine salts, any morphine is carried down in the gelatinous precipitate.

A paste was made by the action of hot water on one Gm. of starch. To this was added 20 Cc. of a stock solution of morphine hydrochloride, then 10 Gm. of barium hydroxide dissolved in hot water. The mixture was cooled, diluted to 100 Cc. and filtered through a dry paper. From the filtrate 50 Cc. was taken, acidified, and mixed with 25 Cc. of standard iodine solution. The mixture was diluted to 100 Cc. and filtered. An aliquot portion of the filtrate (50 Cc.) was titrated with sodium thiosulphate solution.

Volume of sodium thiosulphate solution used = 3.6 Cc. In a blank experiment the corresponding result was 3.4 Cc.

The difference corresponds to 0.0011 Gm. of anhydrous morphine in the fraction titrated, or 0.0044 Gm. of the total original amount.

Combined Action of Lead Salts and Barium Hydroxide on Morphine. Experiment 16.—A few Cc. of basic lead acetate solution was added to 25 Cc. of the same stock morphine hydrochloride solution used in Experiment 15: Barium hydroxide solution was added in excess till the total volume was 250 Cc. The mixture was filtered. One hundred Cc. of the filtrate was acidified and 25 Cc. of standard iodine solution was added, then enough water to make up to 250 Cc. The periodide was filtered out and 125 Cc. of the filtrate titrated with standard sodium thiosulphate solution. A blank determination of morphine was made at the same time.

Sodium thiosulphate solution required

(i) In main experiment ..... 7.6 Cc.
(ii) In blank experiment ..... 3.4 Cc.

Since 1 Cc. $Na_2S_2O_3$ sol. = 1.0638 Cc. iodine solution and 1 Cc. iodine solution = 0.008285 Gm. of anhydrous morphine.

10 Cc. of the stock solution of hydrochloride used above = 0.1464 Gm. of anhydrous morphine, of which amount 0.0735, or more than half, was precipitated by the lead in the foregoing experiment.

The Action of Ammonium Salts on Morphine. Experiment 17.—Crystallized morphine (0.3000 Gm.) was dissolved in standard sulphuric acid and the solution was titrated with standard sodium

hydroxide. The titrated liquid was made faintly acid with hydrochloric acid and then evaporated to small volume. A slight excess of ammonium hydroxide was next added and the evaporation continued to dryness. The residue was drenched with a further small amount of ammonium hydroxide and again warmed on the water-bath to complete dryness. The resulting mixture was dissolved in standard sulphuric acid and titrated with sodium hydroxide solution to determine the amount of free morphine unacted upon by the ammonium salts.

Titration results:

	I Before evaporation with NH_4Cl.		II After evaporation with NH_4Cl.	
Total acid used	25.0	Cc.	25.0	Cc.
Acid equivalent to the alkali	15.0	Cc.	16.7	Cc.
Acid equivalent to the morphine	10.0	Cc.	8.3	Cc.
Weight of free morphine	0.3000	Gm.	0.2490	Gm.

The difference (0.0510 Gm., or about one sixth of the whole) was evidently converted into morphine salt at the temperature of the water-bath.

The Action of Acids on Morphine. Experiment 18.—From a stock solution of morphine hydrochloride 25 Cc. was taken, mixed with 5 Cc. of hydrochloric acid (sp. gr. 1.2) and 50 Cc. of alcohol, and boiled under a reflex condenser for 5 hours. The mixture was then evaporated on a water-bath to about 20 Cc. and the morphine content, as determined by the iodine method, compared with that of 25 Cc. of the original stock solution.

	Sample treated with HCl.	Blank experiment.
Sodium thiosulphate used in titration	9.20 Cc.	9.25 Cc.

Experiment 19.—A. Ammonium hydroxide was added to 25 Cc. of an acid solution of morphine sulphate till it became neutral. It was then acidified with 10 Cc. of hydrochloric acid (sp. gr. 1.2) and the whole was evaporated to about 10 Cc. The solution was then diluted and the morphine estimated by the iodine method.

B. The same volume of morphine solution was treated in the same way as the foregoing, but that 5 Cc. of glacial acetic acid diluted with 25 Cc. of water was substituted for the hydrochloric acid.

A blank experiment was made on the same volume of morphine

solution, its strength being determined by means of iodine without any previous evaporation.

	Volume of $Na_2S_2O_3$ solution used in titration.
Blank experiment	4.50 Cc.
Determination A (after HCl)	4.45 Cc.
Determination B (after CH_3COOH)	4.15 Cc.

The acetic acid itself had no influence on the iodine. When 25 Cc. of the standard iodine solution was allowed to stand for 2½ hours with 10 Cc. of the same glacial acetic acid as that used above, no solid separated. The mixture was diluted and titrated with sodium thiosulphate.

Volume of Iodine solution.	Volume of Acetic Acid.	Volume of $Na_2S_2O_3$ solution required.
25.0 Cc.	10.0 Cc.	25.4 Cc.
25.0 Cc.	0.0 Cc.	25.4 Cc.

Experiment 20.—This was conducted on the same lines as Experiment 19, but sulphuric acid (2 Cc. concentrated acid suitably diluted) was used instead of hydrochloric. The stock solution of morphine sulphate not being the same, a separate "blank" was necessary for comparison of strength.

	Solution Evaporated with H_2SO_4	"Blank" Experiment.
Sodium thiosulphate solution used in titration....	7.7 Cc.	7.4 Cc.

Experiment 21.—This was conducted on the same lines as the foregoing experiments, substituting a considerable excess (about 0.5 Gm.) of salicylic acid for the acids previously used. The stock solution of morphine was not the same.

	Solution Evaporated with Salicylic Acid.	"Blank" Experiment.
Sodium thiosulphate solution used in titration..	17.55 Cc.	17.50 Cc.

The Reactions of Morphine Tartrate. Experiment 22.—A solution was made containing 0.3 Gm. of morphine tartrate (B. P.) in 10 Cc. of water. The following tests were applied to different portions.

A. With ammonium hydroxide, the white crystalline precipitate, characteristic of morphine, was obtained.

B. With iodine dissolved in potassium iodide and water, acidified with sulphuric acid, a characteristic precipitate formed.

C. Potassium-bismuth iodide gave a red precipitate.

D. With dilute iodic acid, iodine was at once liberated.

E. Neutral calcium chloride solution gave no precipitate, but when made slightly alkaline with dilute ammonium hydroxide before being added to the morphine tartrate, a white gelatinous precipitate formed on completion of the mixture. This precipitate had the usual appearance of calcium tartrate.

The morphine tartrate solution was almost neutral to litmus, though distinctly acid to phenolphthalein. It is probably this degree of acidity which prevents the formation of calcium tartrate in a solution not rendered alkaline by ammonium.

SOME OBSERVATIONS ON THE DISSOLVING OF ZINC CHLORIDE AND SEVERAL SUGGESTED SOLVENTS.[1]

By Josiah C. and Bertha L. DeG. Peacock.

The salts of zinc which are soluble in water, especially the sulphate, acetate and chloride, have long been used in injections, lotions, eye-washes, mouth-washes and other such forms of application, usually in weak solutions, a few grains to the ounce.

The sulphate and acetate of zinc readily dissolve in water without residue; but zinc chloride upon contact with water has a strange behavior; and when treated with water in large proportions leaves an insoluble residue known as oxychloride, or basic chloride of zinc; it matters not which is added to the other. This undissolved portion is bulky, therefore impressive as to quantity especially when resulting from one or two grains of zinc chloride intended for eye-drops. That it does contain both zinc and chlorine, we have assured ourselves by qualitative analysis; it may therefore be rightly termed basic chloride of zinc, or oxychloride. Whatever of oxide of zinc or oxychloride of zinc was present in the sample dissolved may also be looked for here.

In order to appreciate the quantity of oxychloride usually left undissolved, let us cite a reference found in the proceedings of the American Pharmaceutical Association, 1896, page 715—"Zinc

[1] Presented at the meeting of the Pennsylvania Pharmaceutical Association, Wilkesbarre, Pa., June, 1918.

Chloride-Dissociation by Water." "Perrot has observed that when zinc chloride, free from oxide was dissolved in water, a precipitate was formed, which had the composition $ZnCl_2$, $5ZnO6H_2O$. An inquiry into the relations of the quantity of water to the amount of oxychloride formed resulted in the determination that by employing 100 mol. of water, 3.25 per cent. of oxychloride was formed, the same quantity was formed with 75 mol., 3 per cent. was formed with 50 mol. and 2.6 per cent. with 25 mol.

The limit of the reaction is, therefore, with 75 mol. of water, the addition of large quantities giving no increase in the yield of oxychloride. *Pharm. Centralh.*, January 23, 1896, 46 from *Bull. Soc. Chim.*, 1895, 975."

Commercial zinc chloride may contain some preëxistent oxychloride as an impurity from overheating in manufacture, and samples of medicinal zinc chloride such as the official grade are expected to show a separation of oxychloride under the condition named; the United States Pharmacopœia accordingly provides a test for limit of oxychloride.

The equation commonly used to explain the change of zinc chloride through the effect of water into this basic salt is

$$ZnCl_2 + H_2O = Zn(OH)Cl + HCl.$$

As already mentioned the precipitate is strikingly bulky, but is by no means a great part of the zinc salt taken. The production of free hydrochloric acid as shown by the equation, is perhaps the reason that all of the zinc is not precipitated by the water. A proper conception of this reaction demonstrates the fact that every clear solution of zinc chloride that is obtained by dissolving zinc chloride in a large quantity of water is a solution of zinc chloride plus hydrochloric acid. This is a matter to be noted toward a better understanding of the behavior of this peculiar substance, for although at this point the statement is largely inference, it will, in due course, become a proven fact.

Even though the undissolved matter is no great part of the zinc chloride, it does of course, represent activity which it is the duty of the pharmacist to vouchsafe to the patient. Therefore, to remove it would be wrong, to dispense it in eye-drops, or similar preparations, would be useless, if not productive of more serious trouble than an explanation.

When first we encountered this behavior we could not take time

to investigate it, so acting under the impression that free hydrochloric acid would be present in any event, as shown by the equation, we concluded that the most practical thing to do was to supply that through lack of which the obstacle arose; in other words, add sufficient hydrochloric acid to the zinc chloride itself to enable the water to carry all of the zinc chloride into solution, realizing as already said, that free hydrochloric acid would be present in the finished product whether all or only part of the zinc chloride was in solution, for this procedure assures the zinc to the patient.

The addition of the hydrochloric acid was made in the case of several grains of zinc chloride by putting a single drop of concentrated acid upon the salt and after mixing by trituration the water was added. When but a grain or two of zinc chloride was to be dissolved, a mere trace or touch of the acid was used, or portion of a drop of diluted acid. Much less acid is needed if put directly upon the zinc salt. Any mixture prepared without this addition and showing turbidity was rejected because too much acid would have to be added to the fluid. The effect of the acid added is to produce zinc chloride and water.

$$Zn(OH)Cl + HCl = ZnCl_2 + H_2O,$$

the very material desired in the product. We have often wondered "what better can be done?" Theory would indicate that the hydrochloric acid in the liquid could be neutralized by mixing it with zinc oxide or carbonate and filtering off the undissolved portion. This plan however is neither so accurate nor so simple as it appears when tried on a small lot of eye drops.

Although the plan of adding acid had been used for many years, without any untoward effects, there might have arisen a comparison between the work of dispensers, wherein the reason for such an addition might be difficult of explanation to the lay mind; for although we believed we were acting within the bounds of right judgment, it might not have been possible to satisfy the patient that such was the case. Nor was the patient the only one who might have to be convinced of the commonsense of the plan, as we shall soon learn; and it was this apprehension perhaps, more than any other influence, that persuaded us to look for another solvent.

Since undertaking this study of the subject, we find that others have practiced this method as the only practical means of dissolving zinc chloride.

Indeed we find that this problem had been referred to a commission of apothecaries and physicians in Belgium, because physicians were objecting to the use of the acid. This body discountenanced the use of the acid, and recommended the use of a turbid solution or the clear liquid therefrom, either of which, as has been pointed out. will contain the same amount of free hydrochloric acid, ***produced but not added.*** Referring to the report of this commission, Dr. Paul Wiskirchen, in the *Pharm. Zeitung,* 1899, page 268, states that he finds "the addition of acid is unnecessary. He finds that if it is attempted to dissolve pure zinc chloride in cold water, or if cold water is added to a clear solution of zinc chloride, turbidity is invariably produced, but if the solution is effected with hot water, or if the dilution is made with hot water, clear solutions result, and so remain permanently." This quotation is from the proceedings of the American Pharmaceutical Association, 1900, page 717, for which it was abstracted from the *Pharm. Centralhalle* of August 17, 1899, page 508. In the same Proceedings for 1907, page 850, we find another abstract, which we quote in its entirety.

"Zinc chloride—Simple Method to Effect a Clear Solution. Franz Wippern directs attention to the fact that while pure zinc chloride usually produces a turbid solution when it is dissolved in cold water, it dissolves perfectly clear in hot water and the solution remains clear on cooling. *Pharm. Zeitung,* Li, No. 73, 1906, 807." Wondering whether we had shut our minds to such a simple and efficient agent as hot water, we hastened to try the suggestion, but only to be utterly disappointed, for we found no appreciable difference in either the immediate or prolonged effect of hot or cold water, in dissolving the salt, or diluting concentrated solutions. If there is any perceptible difference in the effect of hot water from that of cold water, it is merely in making the sediment more dense and to settle somewhat faster, perhaps to be overlooked more easily. Not satisfied to record a refutation of these statements without sufficient proof, we made dozens of tests under varying conditions and quantities, but all to no avail. The statements are erroneous. It was now decided to look into the properties of zinc chloride itself as the most rational starting point of our quest.

One of the characters of zinc chloride which should be borne in mind throughout the consideration of this subject is that property of its solutions to turn litmus from blue to red, or, as usually described, its acid reaction. As is well known this property is common

to many of the soluble salts of the metals; we merely want to remind ourselves at this time that it does not indicate free acid. The sample of zinc chloride which was employed for these experiments conformed to the U. S. P. requirements as to limit of oxychloride content and production; it also conformed to the other tests of the same standard. After a number of experiments made more or less at random to determine features which seem to have bearing upon the matter in hand, a series of experiments was outlined through which it was purposed to follow some zinc chloride in order to note its behavior under varying conditions.

Accordingly, a convenient portion of it was placed in a vessel and water added drop by drop with constant stirring. Approximately an equal weight of water dissolved it—the mixture becoming warm as solution progressed—and a practically clear solution resulted. The addition of water in small portions was continued until a decided precipitate made its appearance. These experiments were repeated several times with different amounts of zinc chloride. On an average it required over five times as much water as zinc chloride to produce a permanent turbidity or precipitate. The further dilution of these turbid solutions with water, threw out more precipitate, so the addition of water was continued until to all appearances no more oxychloride was being produced. This condition appeared to be attained when twenty or more parts of water had been added.

One of these mixtures was allowed to settle and the clear supernatant liquid decanted upon asbestos wool. The filtrate was placed upon a water bath for evaporation. The undissolved portion (oxychloride) was washed and boiled with sodium carbonate to separate the zinc and chlorine, both of which were shown to be present.

Before passing on to the consideration of the evaporated filtrate let us observe some of the behaviors of the clear solution of equal parts of zinc chloride and water. The statement is common in works of reference that zinc oxychloride is dissolved by zinc chloride solution; now the fact, that up to a certain dilution a clear solution of zinc chloride is possible must certainly be conceded to be proof of this statement.

The inference then would be that the total acidity of the zinc chloride solution is sufficiently powerful in that certain concentration to hold in solution any oxychloride which existed in the sample as well as to prevent the separation of the incipient oxychloride which will be manifested upon a further dilution.

Looked at from the view point which attaches to precipitated oxychloride another significance to be gathered from this phenomenon is that there is a limit to the ability of the acidity of the zinc chloride solution to hold the oxychloride in solution, and as through gradual dilution this power suffers attenuation the separation of oxychloride progresses until exhaustion is attained when down comes such balance of zinc in the form of oxychloride as the weakened acidity of the solution can no longer hold dissolved.

The present acidity of the solution, must, therefore, be looked upon as the only reason that all of the zinc is not thrown out in preparing clear zinc chloride solutions by dissolving or diluting with water.

That this acidity must be sufficient, though not necessarily of a related form, was proven through a fortunate thought which occurred just before finishing the work upon these tests; namely, zinc chloride can be dissolved in a well-charged carbonic acid water, without residue of oxychloride; and further evidence that acidity is essential was shown by the fact that if this same solution is boiled or agitated to expel the carbon dioxide, the insoluble oxychloride appears. Boiling caused its immediate separation, agitation revealed it but slowly, while quiet maintained a clear solution for over four days; when afterwards the application of heat caused the escape of a few bubbles of gas, and the looked-for precipitate appeared. But for its fleeting nature, what could be better for our need? That there may be a trace of oxychloride yet held in solution by the combined acidities of the zinc chloride and free acid which have ever enveloped it, would be difficult indeed to prove, but it was proven that a clear solution of zinc chloride of greatest strength possible will not dissolve oxychloride which has been previously separated from a solution. A portion of the cold, clear concentrated solution of zinc chloride was mixed with a small amount of zinc carbonate without change in appearance, but upon boiling the mixture the zinc carbonate dissolved. Even after no more carbonate would be taken up the solution retained its power to redden litmus. On the other hand, a clear solution of zinc chloride from which oxychloride has been completely separated by sufficient dilution, did not dissolve zinc oxide or carbonate, even upon prolonged digestion with heat, thus indicating that in this dilution the affinity between the zinc oxychloride and hydrochloric acid as a balanced condition within the solution is greater than between the zinc oxide and hydrochloric acid.

The liquid was evaporated upon the water bath to nearly constant weight. It was now in the form of a thick syrupy liquid; for zinc chloride cannot readily be dried on a water bath under atmospheric pressure. Besides what moisture it retains this syrupy residue would be expected to also contain the hydrochloric acid from the reaction producing the oxychloride from which it had been filtered; later it will be shown that it does contain this hydrochloric acid.

Two series of experiments, with this syrupy residue, were arranged. In the first of these it was mixed with water gradually added and finally increased to a considerable bulk to find that it dissolved clear throughout. It was then re-evaporated under the same condition to a syrupy consistency and again found to dissolve clear; a third such treatment was given it, and a third time it dissolved clear. The reason for its doing so was the presence of a sufficient amount of hydrochloric acid, tenaciously retained throughout the evaporation, to effect solution, as was proven to be the case by treating the syrupy liquid of the second series of experiments with zinc carbonate. When put into the syrupy liquid the zinc carbonate made no demonstration of the presence of acid until the mixture was thinned with just sufficient water to permit of enough motion for reaction. Effervescence then took place with the disappearance of the small amount of zinc carbonate which had been added. More zinc carbonate was now added until in excess, and the solution warmed, gradually but abundantly diluted with water, and filtered. The clear liquid would now be considered as containing no free hydrochloric acid. Next, it was evaporated to a syrupy consistency on a water bath, and then mixed with water, as had been done in the experiment just preceding it. Instead of dissolving clear as the preceding one, the present experiment gave with first portion of water a clear solution but upon further dilution an abundant residue of oxychloride. This was separated and the filtrate evaporated as before, and upon treatment with water gave a clear solution, thus showing that the acid which was produced in the solution, along with the oxychloride, was sufficient to redissolve all of the zinc chloride. Another evaporation and solution substantiated this opinion. The liquid of the first series was now evaporated for the fourth time, and after it had reached the syrupy consistence, the vessel was placed over a direct flame, and the heat continued, while tests were made from time to time, by removing a drop with a glass

rod, until a point was reached when a drop gave a turbidity with water. This stage was not attained until after and in succession the last trace of moisture which had been held so tenaciously by the zinc chloride and the adhering hydrochloric acid had been driven off and the zinc chloride had been liquefied by the heat, giving additional evidence that adhering hydrochloric acid had been the reason for this syrupy liquid persistently dissolving clear. The fused residue was now treated with an abundance of water and the mixture filtered. This filtrate was evaporated to a syrupy condition as before and found to dissolve clear in water. Another fused mass corresponding to that just described was treated with a limited quantity of water and upon filtering, evaporating and again diluting, oxychloride separated, because when the mass was treated with the limited quantity of water not enough water was present to adjust the acidity so that the full production of oxychloride might take place. The insoluble portions of the fused masses were all shown by tests to be oxychloride.

In order to observe a specimen of zinc chloride which had never been in a solid state and thus avoid oxychloride due to overheating, a concentrated solution was prepared by saturating warm hydrochloric acid with zinc oxide added in excess. The clear supernatant liquid from this mixture precipitated with both hot and cold water and in all respects corresponding dilutions behaved exactly as those obtained from the dissolved salt. One could imagine nothing more likely chemically neutral than this solution prepared by neutralizing the acid with the zinc base; and its precipitation by water must convince the most skeptical that free acid is not only present in every diluted zinc chloride solution prepared with water alone as the solvent, but also that it is needed to insure complete solution.

Neutralize such diluted solution in part, and simultaneously with the precision of natural law readjustment takes place between the zinc chloride and the water present, with the formation of oxychloride and the production of a corresponding amount of free acid; there will be free hydrochloric acid in a diluted solution made with water alone while there is zinc chloride left in it.

Any amplification of these experiments will but reiterate the proven fact, at first but inference—that when this dilution is reached there has been formed and retained hydrochloric acid, and sufficient of it to re-dissolve the residue in any amount of water that may be added.

So much for our study of zinc chloride under the conditions of ordinary manipulation by the pharmacist; and like every definite chemical substance it always behaves the same under identical conditions no matter how often they recur.

Still the problem how to get zinc chloride into solutions of such strength as ordinarily called for in prescriptions without loss, remained unsolved. Left as we were to make the best of what cannot be changed, one might decide, and with sanction of authority, as previously pointed out, to prepare a solution of zinc chloride and ignoring the slight precipitate, ascribe to it an approximately definite strength and of this take sufficient quantity as needed. Such course is perhaps the next best plan to getting the zinc salt entirely dissolved, but the accomplishment of the latter was what had prompted the work; and yet meditation seemed to be but closing the door to possibility.

While reviewing numerous experiences with zinc chloride in prescription work, it was thought that there was a possibility of boric acid being the agent sought. It had been used a great many times in eye-washes with zinc chloride but had never been depended upon for solvent effect. Its suitability to eye washes and its mild acidity, however, strongly urged a trial, and the first experiment showed that it has the very property desired, while subsequent trials established the fact that boric acid will give clear solutions with zinc chloride, grain for grain, in any dilution, hot or cold, up to about twenty grains per ounce. Boric acid applied to the zinc chloride will prevent the precipitation of zinc oxychloride; it will also redissolve a precipitate of oxychloride, although proportionately more is then required than is needed to prevent the precipitate. A saturated solution of boric acid is a convenient form in which to employ the agent, adding it directly to the zinc chloride, or the reverse. Saturated solutions of boric acid at ordinary indoor temperatures contain about twenty grains of boric acid to the fluid ounce; these solutions will dissolve an equal amount of zinc chloride. If such concentrated solutions of zinc chloride are exposed to a lower temperature, they become cloudy, peculiarly so, and though cleared by warmth they do not retain their transparency.

Solution by means of boric acid may also be accomplished by mixing the boric acid intimately with the zinc chloride before the aqueous solvent is applied. This plan involves some allowance for the slow solubility of the boric acid itself. Solutions of zinc chloride

by means of an equal amount of boric acid are permanent, with the exception of the saturated solution as already mentioned. Less than an equal amount of boric acid does not appear to insure permanency.

The limit of solubility of boric acid is the only shortcoming of this agent so far observed. It is of interest to note for subsequent comparison, that upon boiling zinc oxide or zinc carbonate and boric acid together, no zinc enters solution.

While little, if any, objection can be raised to the use of boric acid in this connection, yet because of its limited effect, we sought for another solvent less restricted. Attention had been arrested by a reference to the soluble double salts which zinc chloride forms with ammonium chloride, and effort was turned in that direction. The results with boric acid had strengthened the belief that an acidulated medium is essential to the purpose, and associating this thought with the fact that solutions of ammonium chloride are prone to redden litmus, unquestionably through the presence of a trace of free hydrochloric acid, it was undertaken to learn what effect ammonium chloride would have in the dissolving of zinc chloride. Gratifying, indeed, was it to find the substance a very efficient solvent, and more powerful than boric acid, for applied directly to the zinc chloride one grain of ammonium chloride will dissolve five grains of zinc chloride. If used to dissolve a precipitate of oxychloride an additional amount may be needed, apparently dependent on strength of solution. The solutions with ammonium chloride are permanent.

There would seem to be no objection to the use of the few grains of ammonium chloride which would be needed to prepare an application for a mucus membrane since such parts are constantly saturated with solution of chlorides and likewise inured to the presence of ammonium compounds. Should a very strong solution of zinc chloride be needed as for powerful local effect, ammonium chloride may be depended upon to yield a clear solution.

The possibility of decomposing ammonium chloride in solution with zinc oxide, in the capacity of an alkali and alkaline earth, had not come to mind until now. Upon boiling zinc oxide with a solution of ammonium chloride it was found that the zinc oxide dissolved, of course, with the inevitable liberation of ammonia. Zinc carbonate behaves in this same manner with ammonium chloride. A parallel test with water was made to check up these results against any soluble zinc impurities in the oxide and carbonate. Herein may

be considered to abide the solvent effect of ammonium chloride on zinc oxychloride—an effect again attributable to acidity of medium.

Representing the action by the equation:

$$Zn(OH)Cl + NH_4Cl - ZnCl_2 + H_2O + NH_3,$$

ammonia gas might at first be expected to be in evidence. But when it is recalled that free hydrochloric acid is present or producible in a quantity definitely proportionate to the oxychloride to be dealt with, it is readily understood that no ammonia should be evolved, nor was any, as proven by test.

Sodium and potassium chlorides have no solvent effect upon zinc chloride, but ammonium chloride gives a clear solution of zinc chloride in normal salt solution, and so does boric acid.

A sample of zinc ammonium chloride, was prepared by adding to a solution of zinc chloride of known strength the calculated amount of ammonium chloride to supply an equal number of molecules of the two salts. Crystallization of this solution yielded a product which was recrystallized to obtain the sample shown at this time. The identity of the product was established by tests.

Zinc ammonium chloride forms colorless, transparent crystals, without odor and having an intensely caustic taste. It is readily and completely soluble in water; the aqueous solution is acid to litmus; the solution remains permanently clear. This salt is not an article of commerce in channels through which the pharmacist trades, nor is its use suggested, for the acquisition of it needlessly increases one's stock, especially since boric acid and ammonia chloride must always be at hand.

Since medicated waters are frequently used in solutions for treating conditions wherein zinc chloride is likely to be employed, some experiments were made to observe the behavior of these liquids toward zinc chloride. Peppermint water was found to act as does distilled water; but with boric acid or ammonium chloride yields clear solutions. Camphor water was found to possess acidity sufficient to dissolve zinc chloride up to ten grains per ounce. Beyond that strength camphor water takes on a satiny opalescence due to the separation of microscopic crystals of camphor. The addition of ammonium chloride increases this opalescence. But with or without ammonium chloride these camphor crystals reënter solution within a few days, or immediately upon the addition of a few drops of alcohol. The samples of rose water at our command were

neutral to litmus; they did not dissolve zinc chloride completely until boric acid or ammonium chloride was added. An experience some time past, but well remembered, leads us to believe that specimens of rose water may be encountered which will give clear solutions.

Mucilage of sassafras pith did not dissolve the zinc chloride, until boric acid or ammonium chloride was added; but though the zinc oxychloride went into solution the mucilage was rendered cloudy by its contents.

The statement that zinc chloride forms soluble double salts with some alkaloids as well as with ammonium chloride was tried out with some of those used in eye-washes, with the following results: Equal parts of morphine hydrochloride and zinc chloride did not yield a clear solution, until ammonium chloride was added. Equal parts of pilocarpine hydrochloride and zinc chloride did dissolve clear. Equal parts of cocaine hydrochloride and zinc chloride did not dissolve clear, without the addition of ammonium chloride; boric acid likewise carried the mixture into solution.

Ammonium chloride produced clear solutions when zinc chloride was brought together with morphine sulphate and atropine sulphate.

Our conclusions, from this mass of experiments and data may be summed up in short as follows: the separation of zinc oxychloride when zinc chloride is dissolved in water is always accompanied by liberation of free hydrochloric acid which remains in the solution, at the same time a loss of zinc is experienced. Both of these objections may be overcome in solutions up to approximately twenty grains to the ounce by the use of boric acid weight for weight of the zinc chloride taken. For solutions exceeding this strength, or for any strength, ammonium chloride in quantity of not less than one-fifth of the amount of zinc chloride used, will insure complete and permanent solution. Camphor water will dissolve only a few grains of zinc chloride per ounce. Carbonic acid water may be employed if intended for immediate use. And finally the comparative ease with which a minute quantity of either boric acid or ammonium chloride prevents a precipitate as against the larger quantity needed to redissolve oxychloride once formed may be impressed upon our minds by the wisdom of that renowned maxim: "An ounce of prevention is worth a pound of cure."

THE LEAST THAT SOME OF US CAN DO.

By Henry M. Whelpley,

St. Louis, Mo.

No one escapes having special attention arrested by the world war. This is a crisis in the development of the human race which seriously affects, if it does not actually control our thoughts and activities. All other affairs become extraneous to this cataclysmic action. Some of us have seen too many winters to be of military value. Many are restricted by other conditions. As time passes, the duties for us at home become clearer and clearer. This is a day for patience, courage and endurance; a period of utmost faith and loyalty. All of us must remain one in interest and in sentiment.

Many pharmacists are in the service, more are going soon. They will at once lose their identity as pharmacists. The government will know them only as soldiers and sailors. Let us consider strongly how we can keep alive the fraternal spirit and at the same time aid the boys in developing military efficiency. What better than frequent letters of a cheerful newsy character? This will contribute to contentment and encourage ambition. Show them that we still think of them as pharmacists and are writing because they belong to our calling. This will cause them to place a new value on pharmacy. We would have a pharmaceutical corps in the army today if pharmacists of the past and of this generation fully valued the possibilities of the calling.

But I will avoid being argumentative. This is not the time to ask sharp questions but an occasion for action with one heart. The least that we who remain at home can do is to keep in constant touch with those of our calling whom we know at the front. We must not be divided from our fellow pharmacists even though they are unknown as pharmacists in the army or in the navy.

THE EVALUATION OF BALSAM OF TOLU.[1]

By T. Tusting Cocking and James D. Kettle, B.Sc., F.I.C.

It has been pointed out by several observers that the method of the British Pharmacopœia, 1914, for the estimation of the balsamic acids in balsam of tolu is unsatisfactory. The results obtained are low, as much of the aromatic acid present is combined with resin alcohols and is insoluble in, and thus not extracted by, carbon disulphide.

In 1914 we described a process for the evaluation of benzoin, by which the balsamic acids could be separated from the resinous matter, and the free and combined benzoic and cinnamic acids determined.[2]

The original experiments leading up to this process were carried out on balsam of tolu, and the method was afterwards applied to both benzoin and storax, the results of the former being published.[3]

The method (now official in the British Pharmacopœia, 1914) adopted for the estimation of the aromatic acids in the case of storax[3] was tried on balsam of tolu but abandoned, as repeated extractions by boiling with water caused the resinous matrix to become so stiff and intractable that it was impossible to extract the acids completely.

Boiling out of the aromatic acids with magnesium oxide and water, in the presence of a small quantity of xylene to soften the resinous matter, was found to be the most satisfactory way of dealing with the balsam. The magnesium salts of the aromatic acids are readily soluble in cold water, those of the resin acids being insoluble. A complete separation is effected and the aromatic acids are obtained in a purer condition than by aqueous extraction alone.

The mode of procedure is as follows:

1. *Free Balsamic Acids.*—Five Gm. of the balsam are dissolved in 25 Cc. of hot alcohol in a 250 Cc. CO_2 flask, 5 Gm. of light magnesium oxide, and 20 Cc. of xylene are added, and the flask shaken round until the contents are well mixed. One hundred Cc. of water

[1] Communication to the British Pharmaceutical Conference for publication in the "Year Book of Pharmacy" for 1918.

Reprinted from *The Pharmaceutical Journal and Pharmacist*, July, 1918.

[2] *Y. B. P.*, 1914, 355.

[3] *C. & D.*, March 16, 1912, and May 25, 1912.

are now added, the flask connected to a reflux condenser and boiled for one hour. After cooling, the whole is poured on a Buchner filter, and the aqueous portion of the filtrate separated from the xylene layer, which is returned to the flask together with the filter paper and adhering magnesia-balsam magma. A second 100 Cc. of water is added, and the flask again boiled for an hour, when the aqueous portion of the filtrate is separated as before and the extraction carried out a third time. The bulked aqueous liquids are washed once with 20 Cc. of ether, then rendered acid with hydrochloric acid, and the precipitated acids extracted by shaking out with ether. The greater part of the ether is distilled off, and the residual aromatic acids dried *in vacuo* over sulphuric acid and weighed.

2. *Total Balsamic Acids.*—2.5 Gm. of the balsam are saponified by boiling with excess of alcoholic potash: most of the alcohol is then evaporated off, the residue dissolved in 100 Cc. of hot water, and sufficient hydrochloric acid added to render the whole slightly acid. Five Gm. of light magnesium oxide and 20 Cc. of xylene are next added, and the whole boiled up under a reflux condenser for 1 hour. The aqueous liquid is separated, the extraction twice repeated, and the bulked aqueous liquids treated as in the case of the free balsamic acids.

The proportion of cinnamic acid is determined by the gain in weight on bromination, details of which may be found in our previous note.[2]

The aromatic acids obtained from balsam of tolu are not quite so pure as those from benzoin and storax. The brominated acids from the two latter are white and pleasant smelling, while those from tolu are slightly brown in color, and contain a substance which is extremely pungent and lachrymatory.

Balsam of tolu, as a rule, contains very little that is not soluble in alcohol, but occasionally samples are met with containing woody matter. Three such samples contained 1.6, 8.9, and 9.0 per cent. of insoluble matter.

Moisture, generally present, was estimated by spreading in a thin layer on a sheet of glass and drying *in vacuo* over sulphuric acid. Amounts varying from 2.0 to 8.6 per cent. were found, and the dried balsam was usually quite brittle.

The determination of the acid value of the balsam is somewhat

difficult owing to the dark color, and to the precipitate which is formed on running in the alcoholic potash. We find it best to proceed as follows:

Dissolve 5 Gm. of the balsam in about 50 Cc. of boiling alcohol, add a large quantity of phenolphthalein solution—3 or 4 Cc.—titrate the hot solution with normal alcoholic potash until the color becomes dark brown (but not red), then attach to reflux condenser, boil up for a few minutes in order to break up the precipitate, and finish the titration.

By this method titrations agree to about 0.2 Cc. *N*/1 KOH.

We append a table of analytical data selected to show the variation from a large number of samples of balsam examined during the last few years.

Excluding numbers 11 and 12, which, from their low content of balsamic acids, we believe to have been sophisticated, the figures indicate a range of—

92.2 to 132.4 for acid value,
59.3 to 90.9 for ester value,
154.8 to 206.7 for saponification value,

and 32.68 per cent. to 47.50 per cent. of total balsamic acids.

The pharmacopœial limits for acid value are from 107.4 to 147.2, and for saponification value 170 to 202.

Judged by these figures numbers 3, 4, 6, 7, 8 and 9 would be rejected for low acid values: also the saponification values of numbers 6, 7, 8, 9 and 13 lie outside the limits, although the poorest of these balsams contain 33.87 per cent. of balsamic acids. On the other hand numbers 11 and 12, though abnormally low in balsamic acids, would be admitted as genuine.

We suggest that the pharmacopœial limits be revised, that an improved method for the determination of the balsamic acids be inserted, and also that limits for ester value be adopted in place of those for saponification value. The differences between the extreme limits for acid value and those for saponification value do not coincide with the limits of the ester value.

The experimental work entailed by the above has been carried out in the laboratories of the British Drug Houses, Limited, under the direction of Mr. C. A. Hill, to whom we are indebted for permission to publish the results.

No.	Acid Value.	Ester Value.	Saponification Value.	Per Cent. Free Benzoic Acid.	Per Cent. Free Cinnamic Acid.	Per Cent. Combined Benzoic Acid.	Per Cent. Combined Cinnamic Acid.	Per Cent. Total Balsamic Acids.
1	111.8	71.2	183	8.55	11.99	6.19	5.93	32.66
2	112.3	79.0	191.3	9.12	11.53	7.87	6.56	35.08
3	98.1	79 1	177.2	8.48	11.86	8.35	8.68	37.37
4	100.6	72.1	172.8	7.8	10.69	7.45	8.92	34.86
5	118.2	60.8	179	9.1	13.7	5.94	8.97	37.71
6	92.2	62.6	154.8	6.63	12.4	6.17	8.67	33.87
7	101.3	65.9	167.2	8.29	13.71	5.37	10.13	37.5
8	102.5	59.3	163.8	8.34	13.54	5.22	9.08	36.18
9	96.6	65.0	161.6	7.86	13.12	6 43	9.95	37.36
10	132.4	66.2	198.6	7.42	15.9	11.1	5.2	39.86
11	140.1	39.4	179.5	—	—	—	—	24.74
12	124.3	58.3	182.6	—	—	—	—	24.4
13	117.8	90.9	208.7	—	—	—	—	47.56
14	108.9	85.3	194.2	—	—	—	—	45.12

ALLEGED POISONING BY POTATOES.[1]

By F. W. Harris, F.I.C., and T. Cockburn, F.I.C.

The shoots, haulms, and leaves of the potato contain appreciable amounts of an alkaloid glucoside, solanine; under certain conditions this alkaloidal glucoside may accumulate in the tubers themselves, and may be present in sprouting potatoes in quantity sufficient to cause serious poisoning.

Numerous cases of poisoning have occurred on the Continent. The symptoms of five epidemics in which 716 individuals were involved are recorded by Dixon Mann.[2] Speaking generally, the symptoms were those of gastro-enteritis—namely, vomiting, diarrhœa, colicky pains, headache, depression, etc. The majority of the cases were serious, although all the people affected ultimately recovered. It is to be noted that the potatoes which acted in this way presented no abnormal appearance.

Pfuhl[3] records the poisoning by potatoes in May and June, 1899, of fifty-six men of the Berlin Garrison. The symptoms were similar to the above, whilst jaundice and partial paralysis were noticed in a few cases. A rise of temperature was generally observed, ac-

[1] From *The Analyst*, April, 1918.

[2] Brend, "Handbook of Medical Jurisprudence and Toxicology," p. 252.

[3] *Deutsche medicinische Wochenschrift*, 1899, p. 753.

companied by a feeling of irritation of the throat. No dilation of the pupil was noticed. The suspected potatoes, comparatively few of which had sprouted, were large, white, round, and normal in appearance. As mentioned later, the potatoes were examined chemically, and the proportion of solanine found to be much above the normal.

Mass poisoning by potatoes seems to be comparatively rare in Great Britain. The only case, and that a doubtful one, is reported in Taylor's "Medical Jurisprudence and Toxicology," sixth edition, vol. II, p. 780. The opinion that death (which occurred with two boys who were affected) was due to solanine was based on the fact that in the bowel were found some small pieces of potato peelings which possessed eyes, showing evidence of sprouting. No analysis of the potatoes used appears to have been made.

Towards the end of November, 1917, numerous cases of poisoning occurred in the eastern district of Glasgow; the particulars are shown in the following table, for which we are indebted to Dr. Wright, assistant medical officer of health for Glasgow:

Household.	Number of Persons Ill.	Number who ate Potatoes.	Number who did not eat Potatoes.	Date Eaten.	Onset of Symptoms.	Duration of Illness.
				Nov.—	Nov.—	
A	1	1	7	27, 1 P.M.	27, 2.15 P.M.	Died 31 hours
B.....	8	8	None	24, 1 P.M.	24, 2.3 P.M.	Few hours
C	2	2	1	25, 1 P.M.	25, immediately after	" "
D	2 2	3 (1 ate little)	None	26, 5 P.M.	26, 5.30 P.M.	1 to 2 days
E	2	2	1	26, 5 P.M.	26, 8 P.M.	2 hours to 1 day
F	4	4	1	23, 6 P.M.	23, 24, 25, 5	2 to 3 hours to 2 days
G	7	7	None	24, 2 P.M.	24, 3 P.M.	Few hours
H	3	3	1	25, 12.30 P.M.	24, 2 to 3 P.M.	" "
I.....	2	2	6	24 and 25, 3 P.M.	25, 5.30 P.M.	" "
J.....	6	6	None	23, 1 P.M.	23, 3 P.M.	" "
K....	3	—	—	24, 1 P.M.	24, 2 P.M.	" "
L	1	—	—	23	23, soon after	" "
M....	5	—	1	24	24, " "	" "
N....	4	—	—	23	23, " "	" "
O	2	4	—	23	23, " "	" "
P	4	—	—	24	24, " "	" "
Q	3	—	2	23	24, " "	" "
R	2	—	—	24	24, " "	" "
Total.	61					

The symptoms in the above epidemic corresponded closely to those exhibited in the Continental cases—namely, headache, vomiting, diarrhœa, and debility—one case, that of a boy of five years, terminating fatally. A post-mortem examination showed that death was due to strangulation of the bowel, a condition which, in the opinion of the medical men who conducted the post mortem, might have been caused by extreme retching and vomiting. The viscera gave no indication of irritant poisoning, and no dilation of the pupil was noticed. Investigation showed conclusively that all the persons affected had partaken of potatoes obtained from one source. In some households those persons who did not partake of the potatoes were unaffected, whilst those who did subsequently became ill. The potatoes were purchased in various branches of a coöperative society in the district, and were part of a consignment of thirteen truck-loads which had been supplied to the shops in question.

A sample of the potatoes which had been in use in the household in which the fatal case occurred was procured, and also samples purporting to belong to the same consignment from the shop. As, previous to the post mortem, it was considered that the cricumstances pointed to an irritant poison, these potatoes were examined for mineral poisons, but with entirely negative results. The stomach contents, viscera, etc., from the fatal case were also shown to be free from mineral poisons on examination.

The potatoes were normal in appearance, firm and solid, but some on being cut into sections possessed a brownish indefinite line near the periphery. On standing for a short time the sections of the potatoes developed a much more decided pink color than other samples similarly treated.

As the buds on quite a number of the potatoes showed evidence of sprouting, being about ¼ inch in length, it was decided to determine the quantity of solanine they contained.

The method of G. Meyer[4] was employed for the isolation of the solanine, and is outlined below

500 Gm. of the pared potatoes were finely divided by means of a grater, and the liquid portion separated by pressing in a muslin cloth, the grater being washed with small quantities of distilled water. After standing for some time the liquid was decanted from the separated starch, which was washed with small quantities of distilled water, the washings being added to the original liquid.

[4] *Archiv für Exper. Path. und Pharmakol.*, 1895, p. 361.

After making alkaline with ammonia the liquid was evaporated almost to dryness, and the residue boiled with alcohol and filtered. This treatment with alcohol was repeated twice.

The pressed solid portion of the potatoes was also boiled with alcohol in successive portions and filtered.

The united alcoholic solutions were evaporated to small bulk, allowed to stand overnight, filtered from any asparagin which had separated out, and the filter-paper washed with alcohol.

The filtrate was evaporated to dryness and digested overnight, at the ordinary temperature with 250 Cc. of water containing about 3 Cc. concentrated sulphuric acid, in which the solanine is readily soluble. After filtration and washing the insoluble portion with water the solanine was precipitated with excess of ammonia, the solution raised to about 50° C., filtered and washed, and the solanine dissolved by pouring hot alcohol through the paper. The alcoholic solution was received in a weighed crystallizing dish, the alcohol evaporated off, and the solanine weighed after treating with small quantities of ether and drying in the steam oven.

The sample of potatoes from the household in which the fatal case occurred showed the presence of 0.41 part of solanine per 1,000 parts of potatoes, whilst a sample from the store, supposed to be from the same consignment, gave 0.079 part per 1,000 parts. Wintgen[5] gives the normal content of solanine for potatoes in the month of November as 0.0892 and 0.0880 part per 1,000 parts potatoes. These latter results were obtained by a method which differs from that of Meyer in only a few details.

Meyer[6] found in pared, sound, unsprouted potatoes 0.024 part per 1,000, whilst in potatoes which had commenced to sprout, but were still sound, he found 0.040 to 0.066 part per 1,000.

The solanine was identified by the following tests:

(*a*) Its solution in hot amyl alcohol became, on cooling, a solid jelly.[7]

(*b*) Dissolved in a drop of strong sulphuric acid containing a little Frohde's reagent the color changed to, first, light brown, then reddish, and finally a deep violet color.[7]

(*c*) On heating a minute quantity with a solution of telluric

[5] *Zeitsch. für Unters. der Nahr. und Genussm.*, 1906, p. 113.
[6] *Archiv für Exper. Path. und Pharmakol.*, 1895, p. 361.
[7] "Poisons," A. W. Blyth, fourth edition, p. 397.

acid in moderately strong sulphuric acid (2 water to 1 acid) an intense red color developed.[8]

(*d*) On gently heating a small quantity with strong nitric acid a brownish color was at first developed, then became decided red, and passed suddenly into a pale yellow.

In the Berlin epidemic already mentioned Pfuhl states that the potatoes concerned contained solanine as below:[9]

Pared and uncooked	0.38 part per 1,000
Pared and cooked	0.24 part per 1,000

He gives as the normal content for May and June:

Pared and uncooked (May)	0.060 part per 1,000
Pared and uncooked (June)	0.064 part per 1,000

These figures indicate that in both the Berlin and Glasgow cases the potatoes which caused the symptoms of poisoning contained at least five to six times the quantity of solanine which is found in normal, unsprouted potatoes.

An attempt to detect the presence of solanine in a quantity of the bowel contents of the fatal case was unsuccessful, but this is not surprising in view of the failure of Meyer to detect more than traces in the fæces and urine of a dog which had received 0.1 Gm. of solanine for ten days.

The chemical data obtained in conjunction with the statistics compiled by Dr. Wright demonstrate conclusively, in our opinion, that the outbreak of poisoning was due to the eating of potatoes containing an excessively large quantity of solanine, and indicate the necessity for caution in the use of potatoes which have begun to sprout.

[8] Baur, *Zeitschr. für angew. Chemie*, 1899, 99; *Analyst*, 1899, 24, 152.
[9] *Deutsche medicinische Wochenschrift*, 1899, p. 753.

OITICICA OIL—A NEW DRYING OIL.[1]

By E. Richards Bolton, F.I.C., and Cecil Revis, F.I.C.

During the early part of 1917 we examined a new oilseed sent apparently for the first time from Brazil, bearing the native name of oiticica or oilizika.

The sample consisted of kernels which were oval-shaped and averaged in length from about 2.8 to 4 cm., and in diameter 1 to 2 cm., ten seeds weighing about 35 grms. The kernels readily split into separate portions, much in the same way as do the seeds of *Theobroma cacao,* and, in fact, they closely resemble these seeds in color, being perhaps rather redder in tone, but having a characteristic veining on the outer surface. They have a peculiar and very distinctive smell, which might be described as a heavy and overpowering odor, rather recalling the smell of tung oil, a very interesting property, seeing that the oil, as subsequently described, bears a distinct resemblance to tung oil. There was considerable difficulty in tracing the botanical derivation of these seeds, but it now seems certain that they are the seeds of *Conepia grandifolia,* natural order *Rosaceæ.*

The kernels contain 62 per cent. of an oil, which at normal temperatures is semi-solid, though at higher temperatures the solid portion may be seen to be contained in a medium of liquid oil. The color of the solidified oil is a pale cream-yellow, while the liquid is a bright golden-yellow. The mass solidified with a crenated surface.

The nature of the oil present in the seeds was such that special arrangements had to be made in order to avoid the absorption of oxygen from the air, which takes place exceedingly rapidly as soon as the oil is in a liquid condition. For this reason the drying and storing of the oil were carried out in an atmosphere of carbon dioxide, and special precautions were taken to avoid oxidation during the measuring of the various quantities for analysis. So long as the oil is in the solid state it does not appear to be so sensitive to oxidation.

The following analytical figures were obtained:

Melting-Point.—As the oil consists of a mixture of oils varying from liquids to hard solids, no definite figures can be given to repre-

[1] From *The Analyst,* July, 1918.

sent the melting-point of the oil, and the points of incipient and complete fusion must both be considered.

Incipient fusion	21.5° C.
Complete fusion	65.09° C.

Iodine Value, 179.5.

Saponification Value, 188.6.

Free Fatty Acids as oleic, 5.7 per cent.

Unsaponifiable Matter, 0.91 per cent.

Sp. Gr. at 15.5°/15.5° C., 0.9694.

Refractive Index at 40° C. Zeiss, beyond the scale of the Zeiss butyro-refractometer.

Hexabromide Test.—Only small traces of hexabromides separated when carrying out the test in the ordinary way, but the solution on standing at ordinary temperature for two or three days turned a deep brown color, and precipitated a pale liquid which was not further investigated.

FATTY ACIDS.

Melting-Point	Incipient fusion	53.7° C.
	Complete fusion	67.0° C.
Titer Test		42.8° C.

An attempt was made to separate the liquid fatty acids and obtain their iodine value, but the difficulties involved in attaining the separation of these acids without oxidation proved so great as to render the results unreliable.

In order to obtain some idea as to the value of the oil to the varnish and paint maker, the following experiments were also carried out:

1. *Heat Polymerization Test.*—The oil was heated to a temperature of 250° to 270° C. in an atmosphere of carbon dioxide (in order to avoid oxidation) for thirty minutes, during which time no solidification took place, though a sample of tung oil treated in the same way solidified. It was noticed, however, that during the heating very small bubbles of gas commenced to form as soon as the temperature reached 190° C., but it was not until the temperature reached 280° C. that these bubbles increased to a noticeable extent. Upon reaching 300° C. very large bubbles were evolved, and the

mass set (polymerized). The mass so formed was a *stiff, clear, transparent jelly,* which swelled up indefinitely when mixed with an oil such as linseed or a solvent such as chloroform, and, although no solution apparently took place, the whole mass became gelatinous. It should be noted that the jelly formed by this oil is, as stated above, clear and transparent, while that formed by tung oil under similar conditions is of a distinctly turbid nature. The quantity of oil at our disposal did not allow of any examination of the gas evolved on polymerization.

2. *Oxidation Tests.*—A portion of the oil heated in a thin film at 100° C. for three hours gained in weight 4 per cent. Further heating up to twenty-four hours only showed a total gain of 4.5 per cent. The skin produced in this way is practically insoluble in petroleum spirit, chloroform or acetone. (Tung oil, when treated in the same manner, only increased by 2 to 3 per cent. in weight.) As the oil dries the surface becomes much wrinkled, and there is evidently considerable increase in volume, as is usually the case when such solidification takes place.

A solution of the oil in commercial benzene, when allowed to dry in a thin film on glass, produced a uniform skin, more transparent and continuous in character than is the case with tung oil.

3. *Metallic Driers.*—One or two experiments were tried in this connection, but were not carried out in an exhaustive manner. On the addition of lead acetate to an alcoholic solution of the sodium soaps, a lead compound is formed, as in the case of tung oil, but the substance so produced is of a more granular character than in the case of that oil. These lead compounds are soluble in hot linseed oil when mixed with it in small quantities.

The above experiments all tended to show that this oil has very remarkable properties, which place it in a distinctly unique position, and there seems every reason to suppose that the oil is worthy of the attention of the varnish-maker, and possibly also of those interested in the manufacture of linoleum, but for these purposes it will be necessary to obtain the oil on a commercial scale. Though, as has been pointed out above, special precautions were taken to obtain the oil in an unaltered condition, this was rather for the purpose of obtaining correct analytical figures, and it is quite possible that the oil could be expressed in the ordinary way without serious deterioration, particularly if it were solidified as rapidly as possible after leaving the presses. Even in the liquid condition there is no doubt

that a protective film would form on the surface and prevent further change in the bulk.

We desire to express our thanks to Messrs. Booth and Company, London, Limited, and Messrs. J. H. Rayner and Company for the specimens of the seeds upon which our experiments were carried out.

INDIAN BELLADONNA ROOT.[1]

By E. M. Holmes, F.L.S.

For some years past, belladonna root imported from India has replaced the English root in British commerce to some extent, on the ground that the root presented no perceptible difference to the ordinary observer, and that it yielded a somewhat higher alkaloidal percentage. That belladonna root should be imported *in quantity* from India seemed to indicate a new departure, since it is not an article met with in the Indian bazaars, it is not mentioned by Dr. Dymock in his "Materia Medica of Western India," nor in the works of "Mooden Sherff and U. C. Dutt." Dr. (now Sir) George Watt, in his "Dictionary of the Economic Products of India," Vol. 1, p. 352, points out: "It is a remarkable fact that while this most useful plant is exceedingly plentiful in many parts of the western Himalayas, its medicinal virtues seem to have escaped the detection of the natives of India completely. . . . Not a single leaf or root of this most valuable drug can be purchased, of Indian origin, in the native drug shops of the plains. It would therefore appear that the natives of India have been made familiar with the virtues of this plant in the form of an imported drug, while the Himalayas might supply the world with belladonna." But he further remarks that "the leaves of the Indian plant are a little more acuminate in the Himalayan than in the European plant. This is probably what has given origin to *Atropa lutescens* Jacquemont." Dr. Watt has evidently followed the authors of the "Flora of British India," in considering the *Atropa lutescens* of Jacquemont to be a form of *Atropa Belladonna* Linn.

But even supposing that the two plants are identical, there was

[1] Reprinted from *The Pharmaceutical Journal and Pharmacist*, August 31, 1918.

no evidence in 1889 (the date at which Dr. Watt's remarks were published) that the root of the Himalayan belladonna was met with in Indian commerce. A careful examination of the roots of the Indian belladonna in commerce in this country in 1917 showed me that a large proportion of them differed from the English root in the appearance of the transverse section; whilst in a few samples no such difference could be detected. Under these circumstances, I applied to Colonel Sir D. Prain, the present director of the Royal Gardens at Kew, who resided for some years in India as director of the Botanic Gardens at Calcutta, and inquired if he had any information on the cultivation of belladonna in India; and in reply he kindly gave me the following extracts from the Annual Report of the Kumaun Government Gardens, 1909–10 (p. 3): "Although the plant is said to be exceedingly plentiful in many parts of the western Himalayas, I have been unsuccessful in my endeavors to obtain seed of the Himalayan variety from natives, neither do the large number of hill men I have consulted, including several doctors, know of its existence.

"A small supply (2 ounces) of seed was therefore purchased from Messrs. Vilmorin and Andrieux in August last (1909). The seeds germinated satisfactorily, and, as far as I can judge from growth, the plants are all that can be desired.

"Messrs. W. Ransom and Son, of Hitchin, to whom a sample of hill-grown belladonna root was sent last year (1913), reported it to be of very good quality. I have suggested to the commissioner that fifty acres of virgin forest land be devoted entirely to belladonna cultivation. I have sown large quantities of seed in the Chaubattia nursery, and a good harvest of seed is expected during the coming season from the plants in the Kutcherry Gardens, Naini Tal, which were sown from seed originally imported in 1909 from Vilmorin, Andrieux & Cie., Paris (1914–15 Report).

"In the report of the Economic Botanist (C. *and* D., July 14, 1914), it is stated that the sun-dried roots grown in the Kutcherry Gardens gave respectively 0.4 per cent. of alkaloid from one-year-old plants, and 0.45 per cent. from two-year-old plants; whilst belladonna root obtained from Europe, and used in British medicinal preparations, contains from 0.2 to 0.6 per cent. total alkaloids. The roots grown in Naini Tal are therefore of good average quality, and are suitable for use in the medical store departments of India."

In reply to further inquiries made in December, 1917, by the as-

sistant director of Kew Gardens, Mr. Norman Gill, superintendent of the Kumaun Government Gardens, on learning that the Indian belladonna was considered in this country as rather richer in alkaloid than the home-grown product, remarks, in his reply, which I have kindly been permitted to see at Kew: "I am of the opinion that its superior quality, if any, is due more to the climate, altitude, and the nature of the soil than to any particular variety. As far as I can remember our belladonna resembles botanically the specimens I collected in the woods near Painswick, Gloucestershire, in 1908, when at home on leave. I have never come across a wild specimen in this country, and the plant is unknown to the natives of these parts.

"As far as I am aware, we are the first to supply the Indian market with cultivated belladonna. About 1,000 lbs. of the dried leaves and roots were supplied last year to Messrs. Smith, Stanistreet & Co., of Calcutta, who may have shipped them to England. The only other source of belladonna from this country, is, I think, from Kashmir. This finds its way into the Calcutta market, and is evidently collected from wild plants."

There is thus evidence that both cultivated *Atropa Belladonna* root of European origin, and wild root of Himalayan origin, have apparently been exported to England.

I have subsequently learned from Messrs. B. K. Paul & Co., of Calcutta, that "the Indian belladonna roots now in the market are mostly derived from wild sources in the northwestern frontier provinces and Kashmir. The output at present of cultivated Kumaun belladonna is too small, not exceeding 5 cwt. of root and 2 cwt. of leaves a year."

It is clear, therefore, that there are two varieties of belladonna root from India on the London market, but it is not by any means clear which of those two kinds afforded the richer percentage of alkaloid claimed for the Indian root; nor can it be said to be known whether the Indian plant from the Himalayas is only a variety of *Atropa Belladonna,* or a distinct species. I have examined the dried specimens of this plant, which in the National Herbaria at Kew and the British Museum is the *Atropa lutescens* Jacquemont (*A. acuminata* Royle), and am inclined to the opinion that it is quite distinct from the British plant, the leaves being oblong-elliptical, tapering at both ends, and the flowers funnel-shaped, rather than bell-shaped, of a yellow color, and yellow berries. Whilst examining the speci-

mens at Kew Herbarium, Mr. J. R. Drummond, who happened to be there, told me that he had seen the plant growing in the Himalayas, and that no one who has seen the British plant could confound the Himalayan one with it. The color is a paler green, and its habit stiff and erect, the branching being at a more acute angle. It is noticeable also in the dried specimens that the lateral veins of the leaves branch off at a more acute angle. The root also has a distinctly radiate structure, even in the smaller pieces, which is not the case with the British plant.

At all events, it is desirable that experiments should be made at Kumaun on the plant cultivated there, to ascertain whether the average yield of alkaloid is greater in the Indian-grown than in the British plant, also that the *Atropa lutescens* should be examined as to the alkaloids it contains, and the proportion in which they are present. A microscopical examination of the root is already in progress, and if it proves that there is any important difference in the alkaloidal contents of the Indian root, it is hoped that it may be possible to distinguish it even if used in the powdered state; and, if superior, that its value should be recognized. It may be pointed out, in conclusion, that the *Atropa Boetica* of Wilkomm, which occurs in Spain, bears some resemblance in its yellow flowers to those of *A. lutescens,* but the leaves are ovate, rather than elliptical.

PATCHOULI PRODUCTION IN STRAITS SETTLEMENTS.[1]

By Consul George L. Logan.

Patchouli is both a wild and cultivated crop in the Malay Peninsula. The following data concerning it were furnished to the Penang consulate by the Director of Agriculture for the Federated Malay States:

"Patchouli (*Pogostemon patchouli*) is a soft-leaved herb from 2 to 3 feet high, much branched, with square stems, emitting when rubbed the characteristic smell of patchouli. The Chinese, who chiefly cultivate this plant in Malaya, often plant it on newly cleared ground among the fallen logs. Here, slightly shaded, it grows very rapidly and well. Where it is regularly cultivated, it is planted in properly prepared beds.

[1] Commerce Reports, September 14, 1918.

"The best method of propagation is by cuttings of young shoots. These are cut about 3 inches long, care being taken to cut just below a joint. The cuttings are then pricked into nursery beds well watered and shaded. In three weeks to a month they will have rooted and can be removed to the permanent beds, where they should be shaded until thoroughly established. The plant grows well in open sun, but it will also stand a little shade and may be grown as a catch crop in young rubber or coconut clearings. The cuttings may be planted at distances of about 2 feet.

"*Harvesting and Drying—Marseille and New York Chief Buyers.*—The first crop can be cut six months after planting and afterwards twice a year. In Perak it is usual to take only three crops and then replant. The leaves when cut out may be dried in the sun, but it is better to dry them in the shade, spreading them out in a cool and airy shed. When quite dry (about one week) they may be packed in bales.

"One picul (133⅓ pounds) of the leaf dried just as it is cut yields from 24 to 30 ounces of essential oil, and a sample free from the heavier stalks yields about double that amount. Thirty-six pounds of green leaves produce 10 pounds of patchouli. One-twentieth of an acre planted by Curtis gave 449 pounds of green stuff, and after ten days it had dried to 106 pounds, which on picking over gave 69 pounds good leaf and 37 pounds refuse.

"The dried leaf is exported from this country principally to Marseille and New York. Exports from Penang for 1916 were almost exclusively to New York and amounted to about 65 tons."

The export of patchouli leaves from Penang to the United States during 1917 totaled 79,979 pounds, valued at $12,252 gold. Local exporters of native products are in position to handle a much larger volume of trade in this commodity if orders are received.

JAPANESE AGAR-AGAR.[1]

The manufacture of agar-agar is, as a rule, begun towards the close of the year, and is finished at the end of February. It was started some three centuries ago, but still there is no departure from the primitive method of production. Nor is it systematized or developed into a factory industry, although a new company has re-

[1] From *The Chemist and Druggist*, June 8, 1918.

cently been projected to combine many private and small concerns. Therefore no accurate and up-to-date estimate of its production can be obtained, but it is said that the total value of the annual production is, roughly, 3,000,000,000 yen. In Japan itself only a small portion of the output is used in foodstuffs, the bulk being exported. In 1915 the shipments were 2,202,613 lb., valued at 1,706,064 yen, but in 1916, owing to increased demand and rising prices, the value reached 2,446,862 yen, while the volume stood at 2,785,710 lb. Last year the shipments fell to 2,102,629 lb. and the value to 1,954,983 yen. Before the war China and Germany were the largest buyers, but since the war the United Kingdom, Russia, and China have been the largest buyers; now the United States hold the first position. As to the after-war prospects, the Japanese Government issued a hopeful statement some time ago in one of its reports, but much doubt is entertained respecting this year's trade.

THE PHARMACY DEPARTMENT OF THE AUSTRALIAN ARMY MEDICAL CORPS.[1]

The Australian Pharmacy Department of the A. M. C. (writes Mr. G. E. Gibbard, editor of the *Canadian Pharmaceutical Journal*) is the first independent pharmacy department organized in any army of any state in the British Empire, or even any Anglo-Saxon country, and although in operation barely two years, has "made good" so effectively that its influence is expected to produce a reform in the armies of the entire empire.

The organization is simple and effective, including in its operations both the home and overseas forces.

The members of the pharmacy corps are exclusively qualified pharmacists, enlisted under conditions similar to those which prevail with the other units of the A. M. C., physicians, dentists and veterinaries. The officers are:

Senior major, who ranks as staff officer of pharmacy service on the staff of the director-general of the A. M. C. This position is now held by Major Cossar, who was first appointed Hon. Captain, promoted to Hon. Major, and again to full ranking major.

Next in rank is captain. The chief senior pharmacy officer of each state.

[1] Reprinted from *The Australasian Journal of Pharmacy*, July 20, 1918.

Lieutenants are qualified pharmacists, head dispensers in general hospitals, base hospitals, and forward casualty stations.

Staff-sergeant is the lowest rank of any member of the unit, and is held by all assistant dispensers, and men in charge of medical stores.

Senior major, the officer commanding, is responsible for all medical supplies and through him all recommendations for purchases must be made.

Captain, as chief senior officer of the state, has charge and supervision of all medical stores and supplies for his state.

Lieutenant has charge of medical supplies of hospitals, casualty stations and is chief dispenser for such institutions.

Staff-sergeant is assistant dispenser under command of the lieutenant and A. M. C. quartermaster.

All officers in the pharmacy department must be regularly qualified pharmacists, and draw pay according to rank, as in all other units.

In addition to the above outline, the department manufactures all galenicals required for the service, such as tinctures, elixirs, ointments, liquors, etc. As non-taxed alcohol is used, the saving to the government is very considerable.

CORRESPONDENCE.

SOME REASONS WHY EVERY RETAIL MERCHANT SHOULD KEEP BOOK ACCOUNTS.

Attached is a general letter addressed to retail merchants by the Commissioner of Internal Revenue pointing out the necessity for keeping accounts. Your assistance in the distribution of this letter through the medium of your publication or by duplicating it and mailing copies to your members or customers will be appreciated.

To Retail Merchants:

The Revenue Act now pending in Congress is expected to produce $8,000,000,000. This means a tax on the average of more than $76 for every man, woman and child in America. The average per family is nearly $340.

In many businesses taxes will be one of the largest items of ex-

pense. It is of the utmost importance, therefore, that every concern in business, large or small, whether corporation, partnership or individual, shall maintain an exact record of its receipts and expenses—in other words, keep accurate accounts. Taxes should be considered as an expense of the year for which they are assessed rather than for the year in which they are actually paid and the necessary reserves should be provided for at once.

Because of the large amounts to be collected, the Bureau of Internal Revenue will be compelled to check the income tax returns filed by taxpayers more closely than heretofore. The retail merchant who is able to place before the Internal Revenue Inspector book records showing exactly how he arrived at his statement of net income will greatly facilitate the government's task of collecting the war revenues and save himself annoyance and expense.

No special system of accounts is prescribed by the Internal Revenue Bureau but the books should show in detail inventories, purchases, sales, capital investments, depreciation, and similar items required in making up the income tax return. Every merchant should study the income tax law and regulations and see to it that his accounts are kept in a manner that will enable him to determine his net income for taxation purposes.

Aside from the necessity of keeping systematic accounts in order to comply with the government's requirements, every progressive merchant should adopt an approved accounting system for the good of his own business. In no other way can he further his financial interests more effectively. It has been proven time and time again that accurate accounts are absolutely essential to success in business. The merchant who has a good accounting system is able to eliminate waste and unnecessary expense and can so control his purchases and his credits as to greatly lessen the chance of failure. The inventory, which cannot be taken without some form of accounts, is the compass of a business. Without it the direction in which the business is heading either for success or failure cannot be determined.

In the complexities of modern business costs must be calculated with certainty in order to determine what the selling price of an article should be in order to yield a reasonable profit. This is impossible without books of account.

The profits of a business or the losses of a business cannot be determined without book records; and now that the nation requires every citizen to contribute to the war budget within his means and

income, the returns required by the government under the revenue laws cannot be made with any degree of accuracy without books of account and annual inventories.

The bad-debt loss of the nation, which runs into large figures annually, is due in large measure to inexperience and inability. If merchants would keep even the simplest books of account the bad debt wastage would be reduced materially, for inability and inexperience are usually marked by the absence of an accounting system.

Owing to the withdrawal of man power from industry it is essential that every business man be more frugal and exert himself more effectively to conduct his business efficiently. Extra effort put forth in carrying on the business so as to increase volume at less expense, will decrease the chance of failure, increase the earnings of the merchant as a reward for his effort, and enable him to share more liberally in the governmental financial program made necessary for the successful prosecution of the war.

The man who knows the exact condition of his business from day to day has an immeasurable advantage over the individual who has no records upon which to base his operations. It is the duty of every citizen especially in these war times to keep in such close touch with his business through record keeping and otherwise as to maintain the greatest efficiency and render to his government every cent due in taxes.

DANIEL C. ROPER,
Commissioner of Internal Revenue.

PROFESSORS COOK AND LAWALL SUCCEEDING EDITORS OF REMINGTON'S "PRACTICE OF PHARMACY."

MR. GEO. M. BERINGER,
American Journal of Pharmacy,
145 N. 10th Street,
Philadelphia, Pa.

Dear Sir: We enclose an important note regarding the editorial staff of Remington's "Practice of Pharmacy." The appointment of Prof. E. Fullerton Cook and Prof. Chas. H. LaWall, to continue Prof. Remington's great work will, without doubt, be of great interest to your readers, a large number of whom look to his "Practice of Pharmacy" as the standard work of reference and reliability in its field. They will recognize in these appointments, which were

made by Prof. Remington himself some time before his death, a guarantee of the permanent high standing of this invaluable work.

We hope it will be possible for you to make use of this note on your editorial page, in this or a similar form, as a matter of general interest and importance. With appreciation of any use you may make of it, we are, Very truly yours,

J. B. LIPPINCOTT COMPANY,
ADVT. DEPT.

The sixth edition of this standard treatise on pharmacy appeared only a few months before the death of its famous author and it stands as one of the crowning achievements of that remarkable life. Urged several years ago to relinquish some of his many activities, he yet felt that duty required him to maintain a guiding hand until the new editions of the United States Pharmacopœia, "Practice of Pharmacy," and the Dispensatory were completed—but then the strong will collapsed and in a few months the pharmaceutical world mourned the death of this great leader.

However, with Professor Remington's foresight and attention to details, he had anticipated the inevitable and long planned his succession in the work which was his chief delight, his text book on pharmacy. This was foreseen by many, since for years he has been training and coaching his assistants, and trying out their qualifications on successive editions, until, when sickness compelled him to drop many phases of the work, they were able to carry it to completion.

It is therefore, no surprise to learn that the future of Remington's Practice of Pharmacy will be ably taken care of by E. Fullerton Cook, and Charles H. LaWall, both of whom are already well known in pharmacy and whose selection will insure the continuance of the same high standard and at the same time, the practical character of this famous pharmaceutical guide.

THE PENNSYLVANIA BOARD OF PHARMACY.

NOTICE OF EXAMINATIONS.

HARRISBURG, PA., Sept. 10th, 1918.

Examinations for applicants desiring registration as Pharmacist or Qualified Assistant Pharmacist, will be conducted in the

Philadelphia College of Pharmacy, 145 N. Tenth Street, Philadelphia, and the Pittsburgh College of Pharmacy, Corner Pride and Bluff Streets, Pittsburgh, on Friday and Saturday, November 8 and 9, 1918.

TIME AND PLACE.

PHARMACIST EXAMINATION.

Practical Pharmacy—Friday, November 8, 1918.

Class No. 1, at 9:00 o'clock.

Class No. 2, at 11:30 o'clock.

Pharmacy—Friday afternoon, November 8, 1918, 1 to 6 o'clock.

Materia Medica—Saturday morning, November 9, 1918, 9 to 12 o'clock.

Chemistry—Saturday afternoon, November 9, 1918, 2 to 6 o'clock.

ASSISTANT PHARMACIST EXAMINATION—At the Pittsburgh College of Pharmacy, Corner Pride and Bluff Streets, Pittsburgh, Pa., and the Philadelphia College of Pharmacy, 145 N. Tenth Street, Philadelphia, Pa., on Saturday afternoon, November 9, 1918, at 1:00 o'clock.

L. L. WALTON, *Secretary,*
P. O. Box No. 265, Williamsport, Pa.

The following are the sixth and seventh, respectively, of the students or graduates of The Philadelphia College of Pharmacy known at this time to have made the "supreme sacrifice" in the great war.

GEORGE HERBERT BRENNER, a native of York, Pa., a member of the P.D. Class of 1917, and president of the class in its freshman year, was one of the first P.C.P. students to enter the service of the country. He attended the Officers' Training School at Fort Niagara and won the rank of first lieutenant. He became a member of the Aviation Section Signal Corps, and lost his life, August 25, when his machine fell in northern Italy.

WILLIAM HENRY FITZSIMMONS, aged 26, a native of Kane, Pa., was graduated with the class of 1914. For some time he was employed by the Kane Drug Company, and then became a part owner of the business by buying the interest of E. H. Watkins, '89. Last spring he enlisted in the Navy and was sent to the Great Lakes Training Station near Chicago. He died the latter part of September of pneumonia, following an attack of influenza.

BOOK REVIEWS.

A Laboratory Manual of Qualitative Chemical Analysis. By A. R. Bliss, Jr., M.D. Ph.G., Professor of Pharmacology, School of Medicine, Emery University, Atlanta, Ga.; formerly Professor of Chemistry and Pharmacology, Graduate School of Medicine, University of Alabama. Second Edition, Revised and Reset. 194 pages with working tables. Philadelphia and London, W. B. Saunders Co., 1918. Cloth, $2.25 net.

The present book, designed "for the use of students of medicine, dentistry, pharmacy and science" is the result of a thorough revision of the first edition, in the process of which revision changes, deletions and additions were made.

The subject matter is divided into three parts: Part I, dealing with "The Metals or Cations"; Part II, with "The Acids or Anions"; and Part III, with the analysis of unknowns, metals and alloys.

The first chapter of Part I, covering 40 pages, (1) gives a list of the apparatus and reagents needed to carry out the work outlined in the book, together with directions for preparing the reagents, (2) explains the function of chemical analysis, (3) gives a concise outline of the theories involved in analysis, (4) explains solution, osmotic pressure, ionization, neutralization, electrolytic and hydrolytic dissociation, mass action, etc., and the effects these have in reactions, and (5) closes with a group classification of the common metals, bases or cations. Of the remaining fourteen chapters, each of those of even number takes up a group of metals and discusses each metal as to its symbol, atomic weight, valence and most distinctive physical properties, together with tests for the identification of its ions; while each of the odd-numbered chapters treats of the separation of the ions of a group.

In Part II the anions are considered in three groups: Group A, "Precipitated from neutral solution by Barium Chloride"; Group B, "Precipitated from diluted Nitric Acid solution by Silver Nitrate"; Group C, "Not precipitated by Barium Chloride or Silver Nitrate." Three chapters are devoted to tests for the identification of many common anions, and a fourth chapter takes up the systematic examination of unknowns for anions.

Part III treats of the examination of unknowns for both cations

and anions, and of the qualitative analysis of alloys. A two-page "Solubility Table," giving the relative solubilities in water and acids of the compounds of 25 anions with 29 cations, should be of material assistance to the student in identifying any given one of a large number of unknowns.

The language used in the book is concise and clear, the print is clean and sufficiently bold to permit of easy reading when the book is used on the laboratory table, and, all in all, the manual appears to be well adapted to fulfil its intended mission,—that of teaching students how to identify the majority of the substances with which they have to deal in their every-day practice.

F. P. STROUP.

A CRITICAL REVISION OF THE GENUS EUCALYPTUS. By J. H. Maiden, I.S.O., F.R.S., F.L.S., Government Botanist of New South Wales and Director of the Botanic Gardens, Sydney. Vol. IV, Part 4, Part XXXIV of the complete work.

The part of this critical monograph on the Genus Eucalyptus now at hand describes the following species—Eucalyptus redunca Schauer, E. accedens W. V. Fitzgerald, E. cornuta Labill, E. Websteriana Maiden.

The method of presenting the subjects is in conformity with that adopted in the preceding published parts of this classic study and adds descriptions, ranges, affinities, and varieties and uses of the four species described. The plates illustrating these species are excellent and are high-class illustrations of the lithographers art in depicting botanical characteristics.

G. M. B.

OBITUARY.

JOHN A. DUNN.

Mr. Dunn was born in 1840 in St. Louis, Mo., and, from his early boyhood, was the constant companion of his dear friend, Dr. William F. Edgar, of Los Angeles, Cal. Dr. Edgar was U. S. Army Surgeon and before the Civil War was with the U. S. Government Scientific Survey. The deceased, then a boy, traveled with the expedition that was detailed to run the 35th parallel through New Mexico and to establish a U. S. Army Post at Albuquerque. These

were the first white people who had ever penetrated that country. It was during this expedition that scientists first observed the land of the Cliff Dwellers and claimed that the peculiar formation was due to volcanic disturbance, while the men in the command looked on and argued "these things were made by human hands," which we all know was proven later. Wonderful and numerous were the tales this interesting old gentleman related of the primitive American Indian. As he always added, "Still untainted by the inroads of civilization."

It was during this expedition that the government imported camels to accompany the command across the American desert. The journey was hard and strange and the men impatient and often ugly and Mr. Dunn has often told how much he was impressed when early one Sunday morning they espied the green country beyond the Sierras and the great Pacific in the distance. Not one word was spoken but every man fell upon his knees and prayed his thanks to the One who had safely brought them out of that alkali waste. They went on to California and were stationed at the Presidio and for a time at San Diego.

When the Civil War broke out Mr. Dunn came to New York with the troops and was in the government employ as an apothecary. In 1866 he entered the employ of E. R. Squibb and Sons, manufacturing chemists, as superintendent and as such held sway until in the latter nineties he became one of the firm. He was an expert and an authority and was many times referred to as the brain and pulse of E. R. Squibb and Sons. About ten years ago his eyesight failed, but he did not give up active work until five or six years ago. He was up and around as usual the day before he died. He was smitten with a stroke on Thursday night from the effects of which he passed away Friday morning, August 30.

The deceased was a graduate of the New York College of Pharmacy, an alumnus of same, was also a member of American Pharmaceutical Association, and generally attended the conventions, taking an active interest in the proceedings and a part in discussions, imparting much information from his well-stored mind. The Richmond meeting was the last annual meeting that he attended, in 1910. He was buried in the Cemetery of Holy Cross, Flatbush, on Monday, September 2. He leaves a widow, Annie E., and a daughter, Mrs. J. O. Reither, of Lynbrook, Long Island.

GEORGE DEMING TIMMONS.

In the demise of Prof. George D. Timmons, dean of the Valparaiso College of Pharmacy on July 18, the American Pharmaceutical Association has lost another of its valuable members and an exemplary figure in American pharmacy has passed away. Prof. Timmons was born in Warren County, Ind., on August 10, 1867, and was educated in the schools of his native state. For about ten years he taught in the public schools and thus laid the foundation by practical experience for later successful work as a teacher and dean of the Department of Pharmacy of the Valparaiso University.

Mr. Timmons was graduated from the Valparaiso College of Pharmacy in 1897 and very soon thereafter was appointed an assistant to the professor of chemistry and pharmacy and in 1907 was made the professor in charge of this branch and in 1912 was elected as dean of the Department of Pharmacy. He also attended the University of Chicago for post-graduate studies.

He was an enthusiastic worker and as an author of several works on chemistry gave promise of much more useful labor in behalf of his chosen calling. He possessed the ability to impart his enthusiasm to his students and colaborers and to this is attributed the success that attended his efforts in behalf of his alma mater. His interest in the public affairs of the city and community in which he dwelt was keen and he served four terms as a member of the City Council of Valparaiso.

At the time of his decease he was engaged with Mess Eli Lilly Co. of Indianapolis. He was stricken with typhoid fever and after a short illness died of this malady in the Methodist Hospital in Indianapolis.